

10-1942

Washington University Medical Alumni Quarterly, October 1942

Follow this and additional works at: http://digitalcommons.wustl.edu/med_alumni_quarterly

Recommended Citation

Washington University Medical Alumni Quarterly, October 1942. Bernard Becker Medical Library Archives. Washington University School of Medicine, Saint Louis, Missouri. http://digitalcommons.wustl.edu/med_alumni_quarterly/20

This Article is brought to you for free and open access by the Washington University Publications at Digital Commons@Becker. It has been accepted for inclusion in Washington University Medical Alumni Quarterly by an authorized administrator of Digital Commons@Becker. For more information, please contact engeszer@wustl.edu.

3573
The

WASHINGTON UNIVERSITY MEDICAL ALUMNI QUARTERLY



PUBLISHED IN THE INTEREST OF
THE UNIVERSITY AND THE ALUMNI

++++++

Research on Encephalitis

++

Retrospect to Early Cancer Research

++

The Origin of Cancer in Man

++

Ageing of the Reproductive System

++

Treatment of Severe Diarrhea in Infants and Children

++

Annual Report of the Dean

+++++++

Vol. VI

OCTOBER, 1942

No. 1

68477



OFFICERS OF THE ALUMNI ASSOCIATION OF WASHINGTON UNIVERSITY SCHOOL OF MEDICINE

President: Dr. Charles A. Stone, '08
Vice-President: Dr. Theodore P. Brookes, '09
Vice-President: Dr. Leslie C. Drews, '29
Secretary-Treasurer: Dr. James W. Bagby, '33
Acting Secretary - Treasurer: Dr. Rogers Deakin, '22

Executive Committee

Term Expires 1943	Term Expires 1944	Term Expires 1945
Dr. William Berman	Dr. William G. Becke	Dr. V. P. Blair
Dr. Curtis Lohr	Dr. Thomas M. Davis	Dr. Lee B. Harrison
Dr. F. E. Woodruff	Dr. George J. L. Wulff	Dr. Theodore Hanser
Dr. M. F. Arbuckle	Dr. Claude Pickrell	Dr. Louis H. Jorstad

EDITORIAL BOARD

WASHINGTON UNIVERSITY MEDICAL ALUMNI QUARTERLY

Representing the University:

Dr. Robert J. Terry, '95
Dr. Alexis Hartmann, '21
Dr. Robert Elliott, '36

Representing the Alumni:

Dr. Louis H. Jorstad, '24
Dr. James W. Bagby, '33
Dr. Leo Wade, '38

Dr. Robert A. Moore, Editor-in-Chief
Dr. Jane Erganian, '41, Associate Editor
Dr. Sam Martin, '41, Associate Editor

Office of the Washington University Medical Alumni Quarterly, 602 South Euclid
Avenue, St. Louis, Missouri

Published quarterly by Washington University, St. Louis, Mo. Entered
as second class matter December 14, 1937 at the Post Office at St. Louis,
Mo. under the act of August 24, 1912.

1942
Washington

The Washington University Medical Alumni Quarterly

VOL. 6

OCTOBER, 1942

No. 1

Research on Encephalitis Carried Out at St. Louis University and Washington University with the Assistance of the Encephalitis Fund¹

In October, 1937, Dr. M. F. Engman, Sr. took the initiative in urging that both Universities join forces in a well organized attack on the problem of encephalitis. Mr. Thomas N. Dysart, President of the St. Louis Chamber of Commerce, became interested. A committee made up of representatives of the two universities was soon formed with Dr. M. B. Clopton as Chairman and Mr. W. B. Parker as Secretary. The Chairman, with strong support from the Chamber of Commerce, clearly explained the need for research to business firms employing large numbers of persons, some of whom are undoubtedly liable to encephalitis. The response from these firms was very generous and encouraging. For three years the committee held meetings, sometimes at Washington University and at other times at St. Louis University. During these meetings plans for research were made, appropriations of the necessary funds were authorized and results were discussed in detail. This naturally led to important informal cooperation, the exchange of materials, of ideas, the expression of hopes and to frequent visits in each other's laboratories. Progress reports were submitted to the donors at intervals. This is the summarizing and concluding report.

I. The Clinical Study of St. Louis Encephalitis

Members of the present committee contributed many publications to the clinical study of St. Louis encephalitis at the time of the epidemic of 1933. This disease was again extensively studied during the second outbreak in 1937.

¹ The body of this paper is the formal report of the Committee. The introduction was written for the Quarterly by Dr. E. V. Cowdry—EDITOR.

A summary of the material secured in this study was presented before the general scientific session of the American Medical Association in May, 1939 by Dr. G. O. Broun (5) of St. Louis University. This material was published in "Oxford Medicine" (6) in 1941. In addition to a full clinical description of St. Louis encephalitis, points of similarity and difference between this form of encephalitis and other types such as lethargic encephalitis, equine encephalomyelitis and lymphocytic choriomeningitis were considered at length.

The fact that sporadic cases of St. Louis encephalitis have continued to appear in the vicinity of St. Louis was proven by studies carried out at both St. Louis University and Washington University during the years 1938, 1939, 1940 and 1941. Such cases were reported by Smith, Lennette and Blattner (50) and by Muether (40).

The fact that individuals in the vicinity of St. Louis other than those who have actually suffered from an attack of the disease have been exposed to the virus has been shown by the investigators in the laboratories of both universities who have examined samples of blood taken at random among the population of this area. After the epidemic of 1933 and 1937, a considerable percentage of positive tests were found (39a).

2. Follow-up Studies of Clinical Cases of St. Louis Encephalitis

In cooperation with members of the Health Department of the City of St. Louis, Dr. Broun of this committee carried out a follow-up study of cases of encephalitis from the 1933 epidemic (3). It shows that but few individuals were permanently disabled as a result of St. Louis encephalitis. The outlook for those surviving the acute attack is good. A similar study was made regarding cases from the 1937 epidemic by Jones and Bozalis (33a). These reports deal with conditions approximately one year after the acute attacks. A report covering conditions found five years or more after the acute attack was given by Dr. Broun in the clinical study already mentioned (6) and a more detailed report is now in preparation for publication (10) (23).

3. Investigation to Determine the Character of the Agent Causing the Disease

At the time of the epidemic of 1933 and prior to the organization of the present committee, the disease producing virus was isolated at Washington University by transmission to monkeys and later was transmitted to mice at the Rockefeller Institute by injecting the animals with an emulsion of infected human brain material obtained at autopsy. Further studies showed that the disease producing agent was a filterable virus, that is, a minute invisible organism which will multiply only in animal tissues, and will not

grow on artificial media like the common bacteria. Its presence can be recognized only by the disease it produces in a susceptible animal or by the anatomical changes which it produces in these animals. These anatomical changes were investigated in the Department of Pathology at Washington University (38).

At the time of the second outbreak of encephalitis in 1937, the question immediately arose whether this was caused by the same virus that had caused the epidemic of 1933. The identity of the virus in the two epidemics was first reported by Broun, Greutter, Muether and Casey of St. Louis University before the meeting of the St. Louis Medical Society in September, 1937 (7). Further confirmatory reports were made before the Society for Experimental Biology and Medicine in October, 1937 by the same investigators (27a) and by McCordock, Smith and Moore (39) of Washington University.

The joint committee for the study of encephalitis was organized at this time.

That the virus will multiply in the embryo chick was first shown in Dr. Julianelle's laboratory at Washington University. Smith, of Washington University, attempted to modify the virus by growing it for a long period in the chick egg (46). Although the virus was kept alive in eggs for many months it did not change its behavior. It did not become more infective for the chick embryo and did not lose its infectivity for mice.

Lennette and Smith demonstrated that the St. Louis virus could multiply in tissues of the mouse other than in the brain. When injected into the testicle it multiplied in this organ to almost as great extent as when injected into the brain tissue, but only occasionally produced recognizable disease (34) (35) (48).

The virus of St. Louis encephalitis was compared with the virus of Japanese encephalitis (35) (49) (51) (52). The two were found to be strikingly similar in their behavior and apparently related to each other although not identical. The comparison of these two viruses was carried out at Washington University. Cooke and Blattner (25) (26), also of Washington University, developed a method by which the lesions produced by the virus in the chorioallantoic membrane of chick eggs could be identified more easily by staining with a dye, Trypan blue.

Studies on the method of preserving the virus of St. Louis encephalitis, carried on at Washington University, showed that it could be kept for five or six months in the frozen state and for three months in 50% glycerin. Infective material dried in vacuo was found to be active after periods as long as 17 months (36).

4. Susceptibility of Animals to Infection with the Virus

The virus of St. Louis encephalitis will survive for sometime in the brain of rats and guinea pigs (47). However, the disease can not be established in either species (47) (55). This problem was investigated in both the Department of Pathology and the Department of Bacteriology of Washington University.

Until recently, only mice, monkeys, and chick embryos in addition to man were known to be susceptible to the virus. In 1941, Broun, Muether, Mezera and LeGier of St. Louis University showed that the Syrian Hamster, a larger animal than the mouse, could be readily infected by the virus of St. Louis encephalitis (22). This facilitates the study of the blood tests useful in the diagnosis of this disease to be presently described.

It has been demonstrated by O'Leary, Smith and Reames of Washington University that very young mice are much more susceptible to the infection than are older animals (41). Infant mice die when small amounts of virus are injected into the skin although very large doses of the virus injected in this way do not harm adult mice.

There is no evidence that human infants are more susceptible to the disease than are adults. In fact, the study of the 1933 epidemic seemed to show that the contrary was true.

Because of the suggestion by an epidemiologist during the 1933 epidemic and because of the ease with which the virus multiplied in the chick embryo, chickens were suspected as an animal reservoir for the disease. However, extensive tests of young chickens carried out by Sulkin, Harford and Bronfenbrenner showed that they were not sufficiently susceptible to serve as a possible animal reservoir (56). Broun, Muether and Collier of St. Louis University had been unsuccessful in showing such susceptibility in adult chickens in studies reported in 1934 (16a).

English sparrows captured in the vicinity of St. Louis were examined by the group working in the laboratories of St. Louis University. None were found spontaneously infected with the virus and this species of bird did not prove susceptible to the virus. (Unpublished data.) The same group of investigators also examined a number of bats. Since these animals feed largely on mosquitoes, it was felt that they might harbor the virus if infected mosquitoes were present in this area. No evidence that bats harbor the virus of St. Louis encephalitis was found. (Unpublished data.)

The fact that albino mice are highly susceptible to St. Louis encephalitis naturally led to studies of wild mice as a possible natural reservoir of the infection. In studies carried out at Washington University by Harford, Sulkin and Bronfenbrenner (30), it was shown that wild house mice were susceptible to the infection.

Greutter, Fulton, Muether, Hanss and Broun (29) of St. Louis University showed that two other species of mice, namely, field mice and meadow mice which are common in this vicinity were also easily infected with St. Louis encephalitis. Both groups of workers, however, failed to find any mice actually harboring the virus among those which were trapped. Therefore, while wild mice constitute a possible natural host for the virus, it has not been shown that the mice actually found in the vicinity of St. Louis are spontaneously infected.

5. Possible Methods of Transmission of St. Louis Encephalitis

Four common modes of transmission of epidemic diseases occur: (1) Transmission by actual contact. (2) Transmission by inhalation of infected droplets of water vapor or dust. (3) Transmission by infected food and water taken into the gastrointestinal tract. (4) Transmission by biting insects.

A study of the distribution of cases of encephalitis during the epidemics of 1933 and 1937 by Casey and Broun (24) of St. Louis University showed that a high concentration of cases occurred in rather sparsely populated areas along the streams, open sewers and ponds of St. Louis and St. Louis County during both epidemics. Such a distribution is not that to be expected of a disease spread by human contact or droplet infection, and is the distribution to be expected of a disease spread by a biting insect breeding along water courses, such as the mosquito. It might also indicate that contact with sewerage might be a factor of importance.

The virus of St. Louis encephalitis has not been shown to be infectious to any susceptible animal by simple contact with the skin. Practically no evidence of contact from person to person was found in the epidemics of this disease.

Transmission by droplet or dust infection is possible since the virus can be transmitted by application to the mucous membrane of the nose. But, the absence of multiple cases in the same family and the general distribution of the cases in the city and county are contrary to what would be expected were this the method of spread. However, by the study of cases occurring in 1937 Sulkin, Harford and Bronfenbrenner (54) obtained some evidence for the presence of the virus in the secretion from the nose and throat of patients.

Recently accumulated evidence that infantile paralysis may possibly be transmitted through the gastro-intestinal tract stresses the importance of careful study of this method of infection in the cases of St. Louis encephalitis. Harford, Sulkin and Bronfenbrenner (31) (32) of Washington University have found that feeding infected adult mouse brain tissue

to other mice results in encephalitis only in rare instances. Moreover, Mezera, Broun, Muether and Le Gier (37) of St. Louis University injected infected adult brain suspensions directly into the stomachs or intestines of mice and in only one case did the disease develop. However, Harford, Sulkin and Bronfenbrenner (31) (32) feeding the bodies of infected newly born mice found a different result in that the disease developed in a significantly higher percentage of cases. Wild mice were also shown to be susceptible to infection by feeding of infected newly born tissues. Further experiments indicated that mice which did not die of encephalitis after feeding had some immunity which had probably resulted from inapparent infection. This was analogous to the probable inapparent infection of human beings in nature as indicated by the occurrence of antibodies in the area of many people who have not had the clinical disease. From the above experiments the role played by the gastro-intestinal tract as a portal of entry of the virus remains questionable and only further study of human cases will elucidate the matter.

The virus of infantile paralysis has been demonstrated in sewage in areas where the disease is prevalent. During the summer of 1938, extensive studies of the water of streams, ditches and sewers in St. Louis and St. Louis County were carried out by the group at St. Louis University. In no instance was the presence of the virus demonstrated in these water samples. (Unpublished data.)

Fulton, Gruetter, Muether, Hanss and Broun (27) of St. Louis University, restudied the possibility of mosquito transmission. They found, that by far the most common species of mosquito in this vicinity is the *Culex pipiens*. Working with this species of mosquito captured in St. Louis, they were able to show that when this insect bites an infected mouse, it is able to take the virus into its body and that the virus will remain active. It, however, could not be demonstrated that the bite of these infected mosquitoes could transmit the disease to other mice. As already mentioned, adult mice are not infected when the virus is injected into the skin. The recent demonstrations of O'Leary, Smith and Reames (41) of the susceptibility of newborn mice to virus injections into the skin may point the way to successful mosquito transmission experiments.

That a species of biting insect can transmit St. Louis encephalitis to newborn mice has been shown by the work of Blattner and Heys (2) of the Department of Pediatrics of Washington University making use of the wood tick. The tick can take the virus into its body by feeding on an infected mouse and the disease can be transmitted by such ticks to healthy infant mice. It seems clear that ticks could not have been concerned with the transmission of the human disease in the St. Louis area during the epi-

demics of 1933 and 1937. However, they might be responsible for the spread of the disease among some species of wild animals and thus could keep the disease active in nature ready to infect man when the necessary conditions as yet unknown, are present.

Infantile paralysis virus has recently been shown to be present in flies. The group working in the laboratories of St. Louis University studied a number of species of flies such as horse flies, green flies and the common house fly as well as several species of gnats and other small flying insects. None of these were found to harbor the virus of St. Louis encephalitis and even when raised from the larval stage in the material infected with the virus, it could not be shown that the virus retained its infectious properties in the bodies of these insects. (Unpublished data).

6. Studies on the Epidemiology of St. Louis Encephalitis

An extensive statistical study of the epidemiology of encephalitis was carried out by Broun, Muether, Mezera, Fulton and Ahlering at St. Louis University (17). This revealed certain important facts regarding the distribution of the various types of encephalitis in different parts of the world. It showed that lethargic encephalitis had remained the predominating infection in Europe up to the beginning of the present war. In the United States, this same type of encephalitis was the predominating infection up to 1933. Subsequent to that time, however, the types of encephalitis occurring in the later summer and autumn, the seasonal incidence peculiar to St. Louis encephalitis, and the equine type of encephalomyelitis became the predominating infections.

A study of the statistics for the United States by the same group of investigators (18) showed that the late summer and autumn types of encephalitis probably began to increase in incidence as early as 1930. There is also definite evidence that coincidentally with the St. Louis epidemic of 1933, sporadic cases occurred throughout the greater part of the United States. Indications were found that St. Louis encephalitis coupled with some cases of equine encephalomyelitis remained widely distributed throughout the country since that time. In other words, St. Louis encephalitis is no longer a localized problem, but one of nationwide significance. This material was presented in the form of a scientific exhibit at the meeting of the American Medical Association in Cleveland, Ohio in June, 1941 (13).

This study also revealed the areas in the United States in which late summer and autumn types of encephalitis were prevalent each year. This made possible a comparison with climatological data regarding rainfall and seasonal temperatures in these areas.

This study was made the subject of a Scientific Exhibit at the meeting

of the Southern Medical Association in St. Louis in November, 1941 (14). Two articles (19) (20), now in preparation, will describe these results, showing that excessive heat and drought commonly are found in the regions where late summer and autumn encephalitis are prevalent. A comparison of the epidemiological features of St. Louis encephalitis and poliomyelitis was presented before the meeting of the St. Louis Medical Society in October, 1941 by Broun, Mezera, LeGier and Muether (10).

Data has also been assembled by Broun, Muether, Mezera, Fulton and Ahlerine (21), comparing the distribution of encephalomyelitis in recent years. Broun, Mezera and Muether are engaged in a study of the incidence of encephalitis in the different counties of the state of Missouri. This will serve to define more clearly the extent of the encephalitis problem in this state (15).

7. Serological Tests for the Virus of the St. Louis Encephalitis

The virus neutralization test was first applied to the study of St. Louis encephalitis by Webster and Fite in 1933 at the time they transmitted the virus to mice.

Studies made during the epidemic of 1937 by the group at St. Louis University showed that in some instances antibodies can be demonstrated in the blood of human cases of St. Louis encephalitis within a few days after the onset of acute symptoms (28).

After the discovery of the susceptibility of the hamster (22) to infection with the virus of St. Louis encephalitis, Broun, LeGier, Mezera and Muether (9) of St. Louis University studied the time of appearance of virus neutralizing antibodies in this animal.

In some animals such antibodies may appear as early as 48 hours after inoculation with the virus. These antibodies persist in the animal, certainly for many months. In man, after recovery from encephalitis, they appear to persist indefinitely (28).

A study, similar to that carried out in the hamster, was also carried out in the rhesus monkey by the group working at St. Louis University (8). Here the antibodies appear shortly after inoculation and reach a high titre within a few days after the development of fever. The results in these two species of animals, therefore, is comparable to the early appearance of antibodies as found in human cases of the disease. These studies permit an evaluation of both the use and the limitations of the virus neutralization test as an aid in the diagnosis of St. Louis encephalitis.

Blattner and Cooke (1) of the Department of Pediatrics of Washington University have devised a test for encephalitis making use of the protection of eggs from virus growth by mixing the virus with immune serum prior

to inoculation. The failure of appearance of the typical viral lesion indicates the presence of antibody in the serum.

A very important advance in the serological diagnosis of encephalitis and similar viral infections was made by Roberts and Jones (43) (44) of the Department of Bacteriology of St. Louis University. They have devised a new test dependent on the fact that bacterial cells coated with encephalitis virus may be agglutinated by the sera of animals immunized against this virus and the sera of human beings convalescent from the infection. The advantage of the test lies in the fact that it is much more simple and less expensive to carry out than other virus tests and also the results of the test are available in less than twenty-four hours. This study was carried out by Jones and Roberts of St. Louis University in the case of encephalitis virus, with serum supplied by Dr. Broun, a member of this committee.

Serological tests, using the virus neutralization technique have been carried out by Broun, LeGier, Muether and Mezera (11), of St. Louis University, on a number of cases of post-encephalitic parkinsonian syndrome, a common disabling nervous residual following lethargic encephalitis. All so far tested have given negative reactions for St. Louis encephalitis virus, indicating the rarity of this condition as a sequel of St. Louis encephalitis. Several of the sporadic cases of encephalitis in children studied by Smith, Lennette and Blattner (50) showed severe residuals but none of these cases gave a positive serological test for St. Louis encephalitis.

8. Study of Related Infections Occurring in the Vicinity of St. Louis

A study of St. Louis encephalitis would not be complete if it did not include a study of related conditions which may cause confusion in the diagnosis of this disease.

One such condition is lymphocytic choriomeningitis. This virus has recently been isolated from the spinal fluid of a resident of St. Louis by the group of investigators at St. Louis University (4) (40) and evidence also secured of the occurrence of additional cases. Material is also being collected on the possible presence of equine encephalomyelitis in this vicinity.

Smith, Lennette and Reames, of Washington University, studied and reported a fatal case of encephalitis in a young infant. A virus was isolated from the brain which proved not to be the virus of St. Louis encephalitis but the virus of herpes which has long been suspected of causing encephalitis but has never before been proven to be the cause of a human case of encephalitis (53).

Pinkerton and Henderson (42) of St. Louis University reported a case of toxoplasma infection involving the brain and giving certain clinical findings commonly occurring in encephalitis. Toxoplasma is a relatively rare protozoal disease causing a generalized infection.

Bibliography

1. Blattner, R. J. and Cooke, J. V., The Use of the Egg Protection Test for the Recognition of St. Louis Encephalitis in Man, *J. Infect. Dis.*, 70: 226-230, 1942.
2. Blattner, R. J. and Heys, F. M., Experimental Transmission of St. Louis Encephalitis to White Swiss Mice by *Dermacentor variabilis*, *Proc. Soc. Exper. Biol. and Med.*, 48: 707-710, 1941.
3. Bredeck, J. F., Broun, G. O., Hempelmann, T. C., McFadden, J. F. and Spector, H. I., Follow-up Studies of the 1933 St. Louis Epidemic of Encephalitis, *J. A. M. A.*, 111: 15-17, 1938.
4. Broun, G. O., Lymphocytic Choriomeningitis, Presented at Meeting of the St. Louis Society of Internal Medicine. Mar. 15, 1939.
5. Broun, G. O., Comparison of the St. Louis Type of Encephalitis with other Neurotropic Virus Diseases. Presented before the General Scientific Session of the American Medical Association, May 15, 1939.
6. Broun, G. O., Encephalitis and Other Virus Infections of the Central Nervous System, *Oxford Medicine*, 6: 69-84 (2-46A), 1941.
7. Broun, G. O., Greutter, J., Muether, R. O. and Casey, A. E., The Virus of the 1937 Outbreak of Encephalitis in St. Louis, *Weekly Bull. St. Louis M. Soc.*, 32: 40-43, 1937.
8. Broun, G. O., LeGier, M., Mezera, R. A. and Muether, R. O., The Time of Appearance of Neutralizing Antibodies in the Rhesus Monkey of St. Louis Encephalitis Virus. Presented before the Soc. Exper. Biol. and Med., Dec. 10, 1941. To be published.
9. Broun, G. O., LeGier, M., Mezera, R. A. and Muether, R. O., Immunological Reaction of the Hamster to Inoculations with the Virus of St. Louis Encephalitis, *Proc. Soc. Exper. Biol. and Med.*, 48: 310-313, 1941.
10. Broun, G. O., LeGier, M., Mezera, R. A. and Muether, R. O., Studies of the Epidemiology of Encephalitis. V. A Comparison of the Epidemiological Features of Poliomyelitis and the Summer Types of Encephalitis in the United States, *Weekly Bull. St. Louis M. Soc.*, 36: 68, 1941.
11. Broun, G. O., LeGier, M., Muether, R. O. and Mezera, R. A., Serological Tests for Encephalitis Antibody in Cases of Parkinsonism Observed in the Vicinity of St. Louis. To be published.
12. Broun, G. O., LeGier, M., Muether, R. O. and Mezera, R. A., Occurrence of Lymphocytic Chorio-Meningitis in Areas in which St. Louis Encephalitis is Prevalent. To be published.
13. Broun, G. O. and Mezera, R. A., Epidemiology of Encephalitis, Scientific Exhibit of the Amer. Med. Assn.; *J. A. M. A.*, 116: 1957, 1941.
14. Broun, G. O. and Mezera, R. A., Studies on the Epidemiology of Encephalitis, Scientific Exhibit of the Southern Medical Association; *South. M. J.*, 35: 101, 1942.
15. Broun, G. O., Mezera, R. A. and Muether, R. O., Distribution of Encephalitis in the State of Missouri. To be published.
16. Greutter, J., Broun, G. O., Muether, R. O., and Casey, A. E., Further Studies on the Virus of the 1937 Outbreak of Encephalitis in St. Louis, *Proc. Soc. Exper. Biol. and Med.*, 37: 284-285, 1937.
- 16a. Broun, G. O., Muether, R. O. and Collier, W. D., Transmission of Encephalitis to Mice from Human Brain Material preserved three months in Glycerin and Comparison of this Virus with the Virus of an Epidemic of Tracheobronchitis and Pox present in Fowl in the St. Louis Area simultaneously with the Encephalitis Epidemic. *J. Clin. Investigation*, 13: 701, 1934.

17. Broun, G. O., Muether, R. O., Mezera, R. A., Fulton, J. and Ahlering, J. J., Studies on the Epidemiology of Encephalitis. I. The Seasonal Incidence of Encephalitis with Particular Reference to the Occurrence of the Late Summer and Autumn Types in Large Geographical Areas. Reported to the St. Louis Society for Internal Medicine, Oct., 1941. Demonstrated before Scientific Exhibit of American Medical Association in Cleveland, in May, 1941. Ready to be published.
18. Broun, G. O., Muether, R. O., Mezera, R. A., Fulton, J. and Ahlering, J. J., Studies on the Epidemiology of Encephalitis. II. Localization of Areas in the United States in which Cases of Later Summer and Autumn Encephalitis Preponderated over Other Types. Reported to the St. Louis Society for Internal Medicine, Oct., 1941. Demonstrated before Scientific Exhibit of American Medical Association in Cleveland in May, 1941. Ready to be published.
19. Broun, G. O., Muether, R. O., Mezera, R. A., Fulton, J. and Ahlering, J. J., Studies on the Epidemiology of Encephalitis. III. The Relation of Rainfall to the Occurrence of Late Summer and Autumn Types of Encephalitis. Demonstrated at the Scientific Exhibit of the Southern Medical Association in St. Louis, November, 1941. To be published.
20. Broun, G. O., Muether, R. O., Mezera, R. A., Fulton, J. and Ahlering, J. J., Studies on the Epidemiology of Encephalitis. IV. The relation of Temperature to the Occurrence of the Late Summer and Autumn Types of Encephalitis. Demonstrated at the Scientific Exhibit of the Southern Medical Association in St. Louis in November, 1941. To be published.
21. Broun, G. O., Muether, R. O., Mezera, R. A., Fulton, J. and Ahlering, J. J., Studies on the Epidemiology of Encephalitis. VI. Comparative Distribution of Encephalomyelitis of Horses and Human Cases of Late Summer and Autumn Encephalitis. To be published.
22. Broun, G. O., Muether, R. O., Mezera, R. A. and LeGier, M., Transmission of St. Louis Encephalitis to the Hamster, *Proc. Soc. Exper. Biol. and Med.*, 46: 601-603, 1941.
23. Broun, G. O., Muether, R. O., Mezera, R. A. and LeGier, M., Follow-up Studies of Cases of St. Louis Encephalitis Five or More Years After the Acute Attack. Study completed and to be published.
24. Casey, A. E. and Broun, G. O., Epidemiology of St. Louis Encephalitis, *Science*, 88: 450-451, 1938.
25. Cooke, J. V. and Blattner, R. J., Vital Staining of Virus Lesions on Chorio-Allantoic Membranes by Trypan Blue, *Proc. Soc. Exper. Biol. and Med.*, 43: 255-256, 1940.
26. Cooke, J. V. and Blattner, R. J., Trypan-Blue Vital Staining in Studies of Virus Lesions on Chorio-Allantoic Membranes, *Am. J. Path.*, 18: 163-167, 1942.
27. Fulton, J. D., Greutter, J. E., Muether, R. O., Hanss, E. B. and Broun, G. O., Observations Concerning *Culex pipiens* as a Possible Carrier of St. Louis Encephalitis, *Proc. Soc. Exper. Biol. and Med.*, 44: 255-256, 1940.
- 27a. Greutter, J. E., Broun, G. O., Muether, R. O., and Casey, A. E., Further Studies on the Virus of the 1937 Outbreak of Encephalitis in St. Louis, *Proc. Soc. Exper. Biol. and Med.*, 37: 284-285, 1937.
28. Greutter, J. E., Broun, G. O., Casey, A. E. and Muether, R. O., The Time of Appearance and Subsequent Changes in Titer of the Virus Neutralizing Antibodies in the Course of Encephalitis, St. Louis Type, *J. Clin. Investigation*, 17: 502-, 1938.
29. Greutter, J. E., Fulton, J. D., Muether, R. O., Hanss, E. V. and Broun, G. O., Susceptibility of Field Mice and Meadow Mice to St. Louis Encephalitis, *Proc. Soc. Exper. Biol. and Med.*, 44: 253-254, 1940.
30. Harford, C. G., Sulkin, S. E. and Bronfenbrenner, J., Susceptibility of Wild Mice to the Virus of St. Louis Encephalitis, *Proc. Soc. Exper. Biol. and Med.*, 41: 331-332, 1939.
31. Harford, C. G., Sulkin, S. E. and Bronfenbrenner, J., Infection of Mice by Feeding of Tissues Containing the Virus of St. Louis Encephalitis, *Proc. Soc. Exper. Biol. and Med.*, 41: 332-33, 1939.

32. Harford, C. G., Sulkin, S. E. and Bronfenbrenner, J., Further Evidence Concerning the Transmission of the Virus of St. Louis Encephalitis by Feeding, *J. Bact.*, 39: 70, 1940.
33. Harford, C. G., and Bronfenbrenner, J., Infection of Mice by Feeding with Tissues Containing the Virus of St. Louis Encephalitis, *J. Infect. Dis.*, 70: 62-68, 1942.
- 33a. Jones, A. and Bozalis, G., 1937 St. Louis Epidemic of Encephalitis. Follow-up Studies, *J. Missouri M. A.*, 37: 5-7, 1940.
34. Lennette, E. H., and Smith, M. G., The Propagation of St. Louis Encephalitis Virus in Mouse Testicle, *Proc. Soc. Exper. Biol. and Med.*, 41: 193-194, 1939.
35. Lennette, E., and Smith, M. G., Propagation of the St. Louis and the Japanese B Encephalitis Viruses in the Mouse Testicle, *J. Infect. Dis.*, 66: 266-270, 1940.
36. Lennette, E. H., and Smith, M. G., Preservation of St. Louis Encephalitis Virus, *J. Infect. Dis.*, 65: 252-254, 1939.
37. Mezera, R. A., Broun, G. O., Muether, R. O. and LeGier, M., Intragastric and Intraintestinal Inoculations with St. Louis Encephalitis Virus, *Proc. Soc. Exper. Biol. and Med.*, 48: 357-359, 1941.
38. McCordock, H. A., Discussion of Neal, Josephine B., Types of Epidemic Encephalitis; a Comparison of the Cases Seen in St. Louis in 1933 with Those Seen in New York City, *Am. J. Pub. Health*, 23: 1144-1154, 1933.
39. McCordock, H. A., Smith, M. G., and Moore, E., Isolation of St. Louis Encephalitis Virus during Inter and Epidemic Periods, *Proc. Soc. Exper. Biol. and Med.*, 37: 288-290, 1937.
- 39a. Muckenfuss, R. S., Smadel, J. E. and Moore, E., The Neutralization of Encephalitis Virus (St. Louis, 1933), by Serum, *J. Clin. Investigation*, 17: 53-57, 1938.
40. Muether, R. O., Sporadic Cases of Encephalitis and Allied Infections Occurring during Inter-Epidemic Periods, *Weekly Bull. St. Louis M. Soc.*, 33: 472-475, 1939.
41. O'Leary, J. L., Smith, M. G., and Reames, H. R., Influence of Age on Susceptibility of Mice to St. Louis Encephalitis Virus and on the Distribution of Lesions, *J. Exper. Med.*, 75: 233-246, 1942.
42. Pinkerton, H. and Henderson, R. G., Adult Toxoplasmosis, *J. A. M. A.*, 116: 807-814, 1941.
43. Roberts, E. C., and Jones, L. R., Agglutination of Encephalitis Virus-Coated Bacterial Cells by Virus Antisera, *Proc. Soc. Exper. Biol. and Med.*, 47: 75-76, 1941.
44. Roberts, E. C., and Jones, L. R., Encephalitis Virus "Antibody" in sera of experimentally infected animals by Agglutination of Virus Coated Cells, *Proc. Soc. Exper. Biol. and Med.*, 49: 52-54, 1942.
45. Smith, M. G., and Moore, E., Neutralization of the Virus of St. Louis Encephalitis by Serum from Children, *J. Infect. Dis.*, 64: 319-323, 1938.
46. Smith, M. G., Effect of Prolonged Passage in the Chick Egg on the St. Louis Encephalitis Virus, *Proc. Soc. Exper. Biol. and Med.*, 40: 191-194, 1939.
47. Smith, M. G., Survival of the Virus of St. Louis Encephalitis in Rats and Guinea Pigs, *J. Infect. Dis.*, 64: 307-309, 1939.
48. Smith, M. G., Properties of the Virus of St. Louis Encephalitis in Relation to Its Affinity for Various Tissues, *Weekly Bull. St. Louis M. Soc.*, 33: 471-472, 1939.
49. Smith, M. G., and Lennette, E. H., Comparison of Activity of Viruses of St. Louis and Japanese Encephalitis in the Chick Embryo, *Proc. Soc. Exper. Biol. and Med.*, 41: 323-326, 1939.
50. Smith, M. G., Lennette, E. H., and Blattner, R. J., Etiologic Studies of Sporadic Cases of Encephalitis Occurring in the St. Louis Area in 1938, *Am. J. Dis. Child.*, 59: 509-514, 1940.
51. Smith, M. G., A Comparison of the Viruses of St. Louis and Japanese B Encephalitis, *South. M. J.*, 33: 522-525, 1940.

52. Smith, M. G., and Reames, H. R., Serological Relationship between the Viruses of Japanese B and St. Louis Encephalitis, *Proc. Soc. Exper. Biol. and Med.*, 45: 838-842, 1940.
 53. Smith, M. G., Lennette, E. H., and Reames, H. R., Isolation of the Virus of Herpes Simplex and the Demonstration of Intranuclear Inclusions In a Case Of Acute Encephalitis, *Am. J. Path.*, 17: 55-68, 1941.
 54. Sulkin, S. E., Harford, C. G. and Bronfenbrenner, J., Immunization of Mice by Intranasal Instillation of Nasopharyngeal Washings from Cases of St. Louis Encephalitis, *Proc. Soc. Exper. Biol. and Med.*, 41: 327-329, 1939.
 55. Sulkin, S. E., Harford, C. G. and Bronfenbrenner, J., Attempts to Infect Guinea Pigs with the Virus of St. Louis Encephalitis, *Proc. Soc. Exper. Biol. & Med.*, 41: 329-331, 1939.
 56. Sulkin, S. E., Harford, Carl G. and Bronfenbrenner, J., Attempts to transmit the Virus of St. Louis Encephalitis to Newly Hatched Chicks, *J. Infect. Dis.*, 67: 252-257, 1940.
-

Shortage of Microscopes

It is highly probable that during the next few years students will not be able to purchase new microscopes. Alumni, who have no need for their microscopes, can help in a solution of this problem. Mr. James J. Ritterskamp, Purchasing Agent of the University, will be pleased to hear from alumni and arrange to purchase used modern microscopes.

The Incidence of Leukemia in Children. J. V. Cooke: *J. A. M. A.*, 119: 547-550, 1942.

An analysis of the sex and age incidence of 1,500 cases of acute leukemia in children showed the following trends:

1. During childhood there is a gradual increase in the proportion of males over females who have acute leukemia, the predominance of boys being greater in later childhood than during infancy. In the first year of life more cases were observed in girls than in boys.

2. The age incidence follows a regular curve, which rises from a moderate elevation in the first two years of life to a peak of highest incidence in the third and fourth year, with a sharp decline in the next three years and a more gradual progressive fall throughout the latter half of childhood.

It is concluded that acute infections form one of the factors in the production of the disease and therefore play an important part in its causation, since (1) the highest incidence in acute leukemia occurs in early childhood, (2) the type of its age incidence curve tends to follow the frequency of acute infections in children and (3) some acute infection frequently precedes the development of acute leukemia.

A Retrospect to Early Cancer Research¹

WILLIAM CRAMER, M.R.C.S., D.Sc., Ph.D.

It is a privilege to speak here tonight when you do honor to a man who has won for himself an outstanding position in the history of contemporary medicine. Since the subject of my lecture deals with the later phases of cancer research, I should like to make some introductory remarks about the earlier phases of experimental cancer research, which I hope you will consider appropriate to the proceedings which are to follow.

As a contemporary of Dr. Loeb's, I can speak with personal knowledge and can testify to the trials and tribulations encountered in the early years of experimental cancer research. These difficulties were not only those met with by every pioneer. There was an apathy if not an actual opposition to such work. I came into active contact with cancer research in 1903, two years after Dr. Loeb published his first paper. His name has been familiar to me ever since through his numerous contributions published over the past 40 years. It is difficult today to recreate even in one's own mind the confusion and ignorance in which the cancer problem was shrouded only 40 years ago. But we have as a witness an account written in 1912 by one of the leading English surgeons of that period—Sir Henry Butlin. He had been one of the protagonists of the curability of cancer based on the conception of the local origin of the disease. Butlin worked in the period 1880 to 1910, and in 1912 when he retired he wrote a small book on cancer in which he gives the following account of the conceptions of cancer dominating medical thought and practice up to 1900, and of the change during the next 10 years. After describing the humoral and the constitutional theories of the etiology of cancer, Butlin continues as follows:

“Under this pessimistic pathology the most that was ever expected from an operation was that the patient might die a little less miserably. The disease was often advanced before it was removed, the operation was quite inadequate. . . . There was no hope either for the present or the future. To the very end of their surgical lives many surgeons of the generation before my own were under the influence of these views, and I have heard the expression many times: ‘Once cancer, always cancer’.

“I do not remember when, or where, or how the theory of the local origin of cancer came before the pathologists and surgeons. It was a very happy

¹ Reprinted with permission from the Weekly Bulletin of the St. Louis Medical Society, March 20th, 1942, page 298. Program presented at the St. Louis Medical Society on the evening of the Presentation of the Award of Merit to Prof. Leo Loeb, March 3, 1942.

inspiration, and humanity has reason to be very thankful for it. I have no recollection of discussing it, and suddenly being struck with the belief that it was true. Probably conversion came slowly from the more careful study of individual cases of cancer and from the slow discovery that operations were more successful than they had been believed to be. I can well remember occasionally drawing the attention of the permanent staff (of St. Bartholomew's Hospital) to such successful cases. The reply was always: 'Well, you may be sure it was not a case of cancer.' . . . Gradually belief in the curability of cancer was established. Hope was infused into the minds of surgeons and their patients. . . . It must not be imagined that all this was accomplished without a great deal of opposition, or that it was carried through in the course of a few years. Even when it was evident that the humoral theory could no longer be maintained, it was by no means abandoned. The old humoral pathologists, and those who could not admit the local origin of cancer, spoke of the constitutional origin of cancer; and discussions took place and battle was waged with varying success by the adherents of the two theories, and would probably still be waging had not the question been definitely settled by experimental investigation . . . in the course of the last ten years.

"Since then the local origin of cancer holds the field. The object of the surgeon is to remove it early while it still remains a local disease. . . . His working theory is plain and simple: it is to remove the whole of the existing disease—in fact, to get all the cancer cells out of the body of his patient. If he can do this, the patient will be cured. . . . *The advantages which have been gained for cancerous persons by the institution of a good working theory for a bad one are greater than the mind of man could have conceived.*"

The controversy which Butlin described extended to the attempt to investigate the cancer problem experimentally. It was denied that cancer occurred in animals. It was supposed that cancer was a disease peculiar to man, and especially to civilized man. The attempt to study the disease in such small animals as mice and rates was ridiculed. When I left the Imperial Cancer Research Fund in 1905 to take up a teaching appointment in Edinburgh, I was congratulated by a leading medical man, who happened to come to our laboratory, who said, "You are lucky to get out of a hopeless job." The number of scientific workers who followed immediately the new lead could be counted on the fingers of both hands: Paul Ehrlich and his assistant Apolant in Frankfurt, Borrel in Paris, Jensen in Copenhagen, my chief Bashford and my colleague Murray in London. In this country a Cancer Research Centre was founded in Buffalo with Gaylord at its head and another one at Boston at the Huntington Memorial Hospital,

where Tyzzer worked. This early work on the transplantation of malignant tumors established, as Butlin described, the local origin of cancer beyond the possibility of doubt, and therewith its curability. But when the immediate enthusiasm over the possibility of attacking the cancer problem experimentally had waned and the complexity of the problem became apparent, the old pessimism pervading the medical world prevailed even among some of these early workers. Ehrlich abandoned cancer research and so did Jensen; the Cancer Research Centre in Boston preferred to devote its resources to the investigation of other problems.

But Dr. Loeb, not backed at that time by any financial resources specifically devoted to the cancer problem, held fast to his conviction, that cancer must ultimately yield to scientific research as other diseases had done.

Time has justified his conviction. Throughout those 40 years he has continued to make contributions of fundamental importance to the cancer problem, changing from a lonely pioneer to a leader of an increasing band of workers all over the world. To a scientific worker there can be no finer record than this.

Treatment of Acute Perforative Peritonitis. Robert Elman and C. L. Eckert: *J. Missouri M. A.*, 39: 193-198, 1942.

Perforative peritonitis is largely preventable by removal of the appendix before or as soon after its perforation as possible, by immediate operation on penetrating wounds and perforating lesions, and by careful abdominal surgery. The authors feel that the treatment is essentially surgical, and delayed operation and drainage is less justifiable now than in former years. The change they attribute to introduction of sulfonamides, plasma transfusions and oxygen therapy.

Aniseikonia. Lawrence T. Post: *South. M. J.*, 35: 649-652, 1942.

Aniseikonia, unequal-sized images in the two eyes, was first described in 1863 by Donders. In 1924 Ames, Gliddon and Ogle at Dartmouth devised instruments to measure aniseikonia. Washington University has had such an instrument for eight years and during this time about 800 examinations have been made in the department of ophthalmology. Lenses to equalize the unequal images have been distributed on prescription and then follow-up questionnaires have been issued to determine the degree of relief and satisfaction afforded by these lenses. The questionnaires indicate that the subject is well worth pursuing. The psychologic aspects of aniseikonia and its correction is important.

The Origin of Cancer in Man¹

WILLIAM CRAMER, M.R.C.S., D.Sc., Ph.D.

The title of my paper might be expressed more simply by the question Why does a patient get cancer? This is a question which must have come often to your mind. If a patient presents himself or herself at an early stage of the disease when the growth is still small, the feeding or the seeing of a tumor may have been the very first sign of the disease. There may be no other symptoms, not even pain, the patient is apparently in good health, there is no previous history of any disease or trauma: the disease appears like a "bolt from the blue."

The early workers in cancer research laboratories had the same experience. They kept large numbers of young mice or rats together in big cages on the same diet. After a while one of these animals, which had never been subjected to any experimental procedure, would suddenly develop a malignant growth, then in a second and later perhaps in a third animal a tumor would appear, while the bulk of the animals, though kept under identical conditions in the same cage and on the same food, would complete the natural span of their lives free from cancer. It was thus taken for granted that cancer arises suddenly in a previously normal tissue, and it was this sudden, unexpected and apparently capricious appearance of the disease which gave to it the aspect of a grim mystery. It also gave rise to the conception that the origin of cancer was to be found at the time of the first appearance of a malignant cell.

The attention of students of cancer thus became riveted on the investigation of the nature of the malignant cell as the one and only problem in the etiology of cancer, which became limited to an explanation of the unrestricted growth of the cancer cell. Since it was proved conclusively by the early work on the transplantation of spontaneous tumors in animals that this unrestricted growth was due to a change lying entirely within the cell and was not brought about by growth stimuli acting on the cancer cell from without, the solution of the cancer problem seemed to be confined to an explanation of this intracellular change. And since it seemed justifiable to assume that this intracellular change is the same in whatever tissue or

¹ Reprinted with permission from J. A. M. A. 119: 309-316, 1942.

From the Barnard Free Skin and Cancer Hospital.

Read before the St. Louis Medical Society March 3, 1942, on the occasion of the presentation to Prof. Leo Loeb of the Award of Merit and the Gold Medal of the Society.

Dr. Cramer is research associate, the Barnard Free Skin and Cancer Hospital, St. Louis, and late senior member of the Research Staff, Imperial Cancer Research Fund, London, England.

organ it occurs, cancer appeared to be, from the etiologic point of view, a single disease and the nature of this intracellular change was spoken of as "the cause of cancer." Various lines of attack on the nature of this intracellular change have been followed, but this problem still awaits a solution. What has completely changed the aspect of the cancer problem and opened up new ways and means of attacking it is the recognition that cancer does not arrive suddenly and that the intracellular change represents only one aspect of a very complex problem.

One of the characteristic features of the disease is its age incidence: cancer increases rapidly in almost geometrical progression as age advances. This was explained formerly by the assumption that senile tissues are particularly prone to the cancerous change. When it became possible to produce cancer experimentally, by a variety of carcinogenic agents, it was found that cancer can be induced as readily in a young organism as in an old one. The senility of an organism does not, therefore, account adequately for the characteristic age incidence of the disease. The explanation must be sought elsewhere. It lies in the fact that the intracellular change represents the culmination of a process which occupies a long period of time. This period—the period of induction—is not the same for different species of animals if expressed in units of astronomical time. But there is a striking similarity if we express the results in units of biologic time; that is to say, in equal fractions of the natural life span of each species. The production of cancer by coal tar requires on the average six months in a mouse and fifteen years in man. With a life span of two years for a mouse and seventy years for man, six mouse months represent one-fourth of the life span of a mouse and fifteen human years nearly one-fourth of the life span of man. During this long period of induction the tissue on which the carcinogen acts undergoes a series of pathologic changes involving among other things increased cell division. Eventually this altered tissue passes into a condition in which a few cells within this altered tissue undergo, sooner or later, an irreversible intracellular change which transforms them into malignant cells. When this happens, the scene changes from the exterior to the interior of the cell.

The Origin of Cancer: Proximate and Remote Causes of Cancer

The irreversible intracellular change, when it has once occurred, persists within the cell even after the carcinogenic agent has been withdrawn. The recent work on experimental carcinogenesis has thus in no way changed the fundamental conception that the autonomous infiltrative growth of the cancer cell is a property residing within the cell. On the contrary, it has confirmed and extended it. But it has made it clear that the expression "the cause of cancer," which was used previously, has become meaningless.

As far as the birth of a new race of cells—the cancer cells—has its immediate origin in an intracellular change, this change may be called the proximate cause of cancer. But since this change occurs most frequently—if not always—in a tissue which has undergone pathologic changes as the result of having been exposed to the action of a carcinogenic agent, we must take account of this more remote origin of cancer by distinguishing the “remote causes” of cancer from the “proximate cause” or causes. Eventually, when more is known about the nature of the intracellular change, we may be able to understand the connection between these two problems. At present they have to be treated as two separate and distinct problems requiring a different technical approach and involving different biologic conceptions. The experimental study of the remote causes of cancer has made it possible to interpret a number of hitherto obscure features concerning the origin of cancer in man and to open up ways and means by which this problem can be attacked in the human subject. Since the etiology of cancer involves a consideration of a plurality of remote causes, the term “remote causal factors” seems preferable. These may be conveniently divided into four groups, which will now be discussed briefly. They are:

1. Carcinogenic agents.
2. The precancerous condition.
3. Susceptibility.
4. The time factor.

Carcinogenic Agents

The carcinogenic agents which have so far been identified differ greatly in their nature. They may be chemical substances, physical agents such as roentgen rays, radium rays or ultraviolet light rays, or gross parasites such as *Taenia crassicolis* in rats, *Bilharzia* in man. The chemical substances, of which about one hundred and seventy have been identified, fall into two groups: (1) substances foreign to the physiologic economy of the body and not formed by it normally and (2) substances normally formed by the body and possessing definite physiologic functions. Examples of the first group are tar, dibenzanthracene, benzpyrene and methylcholanthrene. These different chemical substances, which have a mildly toxic effect on the animal organism, vary greatly in their carcinogenic potency. They are locally carcinogenic for the skin when applied to it. When injected subcutaneously they are also locally carcinogenic for connective tissue. They also produce cancer locally at the site of their application in a number of internal organs, including the stomach, intestine and mamma. They may also produce cancer remotely in the lungs, either when applied to the skin or when injected subcutaneously. To this group belong also a number of organic dyestuffs, such as butter yellow, which when ingested with the food are

specifically carcinogenic for one organ, the liver, but not for other organs. The fact that some of the chemical substances known to induce skin cancer in man, such as tar, shale oil and radiations, also induce skin cancer in mice and other species of animals is evidence of the essential similarity of the experimental disease to the disease as seen in man. Although a large number of chemical carcinogens have been synthesized, their mode of action is still obscure. A systematic investigation organized by Dr. E. V. Cowdry is now under way in the Barnard Hospital in St. Louis. One result obtained so far which has a bearing on the etiology of cancer in man is that the exposure of a tissue to the carcinogenic agent need not necessarily be long continued and unremitting, as has been generally assumed. A few isolated exposures to a powerful carcinogenic agent, separated from one another by long intervals of time, can be effectively carcinogenic.¹ Under special conditions even a single exposure of the skin to a chemical carcinogen is sufficient so to alter the epithelium as to send it on its way to the development of cancer.

In contrast to this group is the group of carcinogenic hormones, such as the estrogens. They are formed in the body and fulfil definite physiologic functions. They may be either the actual hormones normally present or organic substances having a different chemical constitution but possessing the same physiologic properties. This means that their carcinogenic effect is tied up with their physiologic action. They are specifically carcinogenic for a group of organs not exposed to agencies coming from without but influenced physiologically by these hormones, organs such as the mamma, the uterus, the prostate and the thymus. They are not carcinogenic for the skin.

Quite recently a number of facts have come to light which indicate that there is a fundamental difference in the mode of action of the chemical carcinogens on the skin and that of the estrogenic hormones on the mamma. The former, which, as already stated, are foreign to the physiologic economy of the body and have a mildly toxic effect on the organism, induce at their first application an injury to the cells of the skin followed by an excessive regeneration. The resultant epithelial hyperplasia is, therefore, an indirect effect. The estrogenic substances, on the other hand, induce a hyperplasia of the mammary epithelium as a normal response of a tissue to its physiologic chemical stimulus. The subsequent development of cancer in the mamma is dependent on the presence of a substance of a high molecular weight, the exact nature of which has not yet been identified. This substance is transmitted from its mother to the individual animal immediately

¹ Cramer, William, and Stowell, R. E.: *Cancer Research* 1:849, 1941.

after birth in the milk. This is the so-called "milk factor" of Bittner.² This milk factor is stated to be present only in strains with a high incidence of spontaneous mamma cancer; it is absent in strains with a low incidence.

While the presence of this milk factor is essential for the induction of cancer in the mamma by estrogenic substances, cancer can be made to develop in that organ in the absence of the milk factor if a chemical carcinogen such as methylcholanthrene is locally applied to the mammary gland. For Strong³ has shown that by this technic cancer can be induced in the mamma of mice belonging to a strain in which breast cancer never develops spontaneously in the females and cannot be induced experimentally in the males by estrogens. Ex hypothesi, the milk factor is absent in such a strain. It follows from this that the origin of cancer in one and the same organ, the mamma, can be due to two widely varying combinations of remote causal factors.

But one fact stands out, whatever the combination of remote causal factors may be and whatever tissue they are allowed to act on a considerable period of time has to elapse before the action of these factors on a given tissue culminates in the development of cancer. What occurs during that period? This leads directly to a consideration of the second item on our list.

The Precancerous Condition

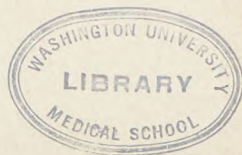
During the prolonged period of induction necessary for a carcinogenic agent to elicit cancer, the tissue on which these agents act undergoes a pathologic change, and it is in this altered tissue that eventually a malignant conditions develops in a sharply circumscribed area. In the two tissues in which experimental carcinogenesis has been studied most extensively—the skin and the mamma—this alteration consists, as far as the epithelium is concerned, in hyperplasia, which in the skin becomes visible to the naked eye frequently, though not always, in the form of papillomas. But it must not be assumed from this that every form of hyperplasia is a precancerous condition or that a papilloma must necessarily develop into a carcinoma. There are, as we shall see, in man certain atrophic conditions of the epithelium which have been recognized as precancerous. The significance of the precancerous condition will be discussed again later.

The Host Factor of Susceptibility

When carcinogenic agents are applied to the skin of animals, they do not produce their carcinogenic effect uniformly; in some animals cancer appears earlier than in others, and in some individuals cancer does not appear at all. These differences become even more well defined when estro-

² Bittner, J. J.: *Am. J. Cancer* 36:44, 1939; *J. Nat. Cancer Inst.* 1:155, 1940.

³ Strong, L. C., and Williams, W. L.: *Cancer Research* 1:886, 1941.



60477
46/44

genic hormones, which are carcinogenic for the mamma, are applied to inbred strains differing in their spontaneous incidence of mammary cancer. The ovarian follicular hormone, which may produce 100 per cent of mammary cancer in the males of one particular strain with a high incidence of spontaneous mamma cancer in the females, may produce no carcinogenic effect at all in the males of another strain in which cancer never develops spontaneously in the mamma. There is, therefore, a factor residing in the host and transmitted to it from its parents which determines the efficacy of a carcinogenic agent. This factor is designated by the intentionally vague term susceptibility. By applying the methods of genetics⁴ to the cancer problem it has been demonstrated among other facts that the factor of susceptibility does not extend to all organs of an individual but is restricted to one particular organ. Thus it is possible to produce by inbreeding a strain of mice with a very high incidence of spontaneous cancer of the mamma, indicating a high degree of susceptibility to cancer in the mamma. But the skin of the animals belonging to such a strain is not necessarily more susceptible to the carcinogenic action of a chemical carcinogen.

The relationship between the two factors susceptibility and carcinogenic agent can be expressed crudely by a simple equation of two variables, A and S , and a constant, C :

$$A \times S = C$$

In such an equation the one variable increases as the other diminishes. If A represents the carcinogenic agent, S the susceptibility and the constant C the carcinogenic effect, the equation expresses the fact that cancer can arise in an organism either with a high susceptibility and a weak carcinogenic stimulus or with a low susceptibility and a strong carcinogenic stimulus. The equation reads therefore

$$\text{Carcinogenic Agent} \times \text{Susceptibility} = \text{Carcinogenic Effect}$$

The Time Factor

There is yet a third variable which enters into the etiology of cancer, the factor of time. A considerable period of time is necessary for a carcinogenic agent to induce cancer even in a susceptible animal, and this prolonged period varies inversely with the strength of the carcinogenic stimulus and with the degree of susceptibility. It is shortest when a strong stimulus is applied to a highly susceptible animal, and it is very long when the two other variable factors have low values. This can be expressed by the equation:

$$\text{Time (Carcinogenic Agent} \times \text{Susceptibility)} = \text{Carcinogenic Effect}$$

This means that the appearance of cancer at an early age indicates a

⁴ Little, C. C.: A. Review of Progress in the Study of the Genetics of Spontaneous Tumor Incidence, J. Nat. Cancer Inst. 1:727, 1941.

strong carcinogenic stimulus or a high degree of susceptibility or a combination of the two. If, on the contrary, the carcinogenic stimulus has been weak or intermittent or/and if the degree of susceptibility has not been high, cancer will develop at later age periods. The longer the individual lives, the greater is the chance that a product of carcinogenic stimulus and susceptibility too weak to elicit cancer in early middle age will become effectively carcinogenic. This accounts for the rapid increase in the cancer incidence rate with advancing age.

The Etiology of Cancer in Man: Cancer a Multiplicity of Diseases

Cancer in man may be considered as an experiment carried out by nature on the human species. But in this case we see only the end results of the experiment. In order to trace the various factors which have taken part in this experiment we must adopt a "follow-down system." The follow-up system, with which we are all familiar, enables us to determine the results of treatment. It tells us nothing about the origin of the disease. The follow-down system is only now beginning to be developed. It attempts to trace the disease in man back to its origins in the light of the knowledge gained from the experimental analysis of the disease in animals.

The first thing to bear in mind in such investigations is the great variety and variability of the etiologic factors. They are different for different organs, and even for one and the same organ there may be a variety of ways in which the several factors are present in combination. We must recognize that from the point of view of the remote causes cancer is a multiplicity of diseases in man as it is in animals. In order to trace the various etiologic factors, the vast bulk of data concerning human cancer has to be broken down into separate groups. I shall try to illustrate this point by discussing briefly the following groups:

Primary liver cancer.

Hereditary factors.

Social factors.

Precancerous conditions.

Gastric cancer.

The hormonal etiology of breast cancer.

Primary Cancer of the Liver

This disease is very rare in Europe and in this country. It is often found in the natives of the Far East and of South Africa,⁵ and, where accurate statistical observations have been available, it has been found that the liver is the organ most frequently affected by cancer. This difference

⁵ The literature is reviewed by Shear, M. J.: *Am. J. Cancer* 29:269, 1937.

has until recently been a remarkable and puzzling phenomenon. Here is the explanation.

Japanese investigators⁶ found that primary liver cancer could be induced in mice and rats by adding certain azo dyes, such as butter yellow, to the diet. Such dyes are used in the artificial coloring of foodstuffs. When the experiments were repeated in European and American laboratories, liver cancer did not develop as readily or failed to appear altogether. Further investigation showed that this discrepancy was accounted for by the fact that the stock diet of the animals in Japan consisted of rice and carrots, while in European and American laboratories the stock diet was more varied and built around wheaten cereals as the basic foodstuff. This difference reflects of course general differences in the respective diets consumed by different races of man in different parts of the world. Further experimental analysis by Rhoads and his collaborators⁷ demonstrated that the two dietetic factors responsible for the difference were casein and a vitamin—riboflavin—belonging to the B complex. When these two substances are added to a diet of rice and carrots, butter yellow does not induce liver cancer.

In the story of cancer research this recent analysis of the etiology of liver cancer is one of the most interesting chapters and it is worth while to consider it in some detail. We have here again two remote causes: a carcinogenic agent—butter yellow—and the susceptibility of the liver to that agent. But in this case the susceptibility factor is not inherited or transmitted from the parent but is dependent on conditions acting on the organism from without—namely the diet. We have here also a striking demonstration of the close similarity existing between the etiologic factors determining the development of cancer in man and in animals. It is true that we have not yet identified the carcinogenic agent responsible for the prevalence of primary liver cancer among the natives of the Far East, but the dietary factor predisposing the liver, and only the liver, to the development of cancer is the same for rats and for human beings. It is therefore justifiable to conclude that liver cancer, as it occurs among the natives of the Far East, can be prevented by dietetic measures.

Familial Incidence of Cancer in Man

When this subject was first studied, the total incidence of cancer of all organs was made the basis of all investigations. For reasons which will become evident, such investigations failed to reveal any pronounced differ-

⁶ Sasaki, T., and Yoshida, T.: *Virchows Arch. f. path. Anat.* 295:175, 1935.

⁷ Kensler, C. J.; Sugiura, K.; Young, N. F.; Halter, C. R., and Rhoads, C. P.: *Science* 93:308, 1941. Sugiura, K., and Rhoads, C. P.: *Cancer Research* 1:3, 1941.

ences of the cancer incidence between persons with and persons without a family history of cancer.

In two more recent investigations carried out independently by Wassink⁸ in Amsterdam and by Waaler⁹ in Norway the material collected by them was further analyzed according to the organ incidence. Since these two investigations are not readily accessible they will be discussed in some detail.

The basis of the material used for such investigation were persons known to suffer or to have suffered from cancer of the various organs. These are called the "basal patients." The next step was to collect information about the incidence of cancer in the near relatives of the basal patients: either the brothers and sisters—"sibs" for short—or brothers, sisters, parents, aunts and uncles. It thus became possible to determine first whether the near relatives of persons with cancer of the one organ develop cancer more frequently than does the rest of the population (table 1).

TABLE 1.—*Proportionate Cancer Mortality in Sibs of Basal Patients with Cancer, Analyzed by Organs (Waaler)*

Percentage Incidence of Cancer in General Population	Lip		Other Sites				Stomach, Liver, Esophagus				Uterus, Breast and Ovaries		Pros- tate	
	B.P. ♂		B.P. ♂		B.P. ♀		B.P. ♂		B.P. ♀		B.P. ♀		B.P. ♂	
	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀
	17	17	17	17	23	22	22	32	32	33	24	30	23	37
													46	9

B.P. = basal patient.

The figures show that the sibs of male basal patients with lip cancer do not suffer from cancer more frequently than the general population. There is a definite increase for the sibs of basal patients with cancer of the esophagus and stomach, and in this group there is a definite sex difference, the brothers of female patients with cancer of the esophagus or stomach showing the lowest frequency in this group. A remarkably high incidence is found among the sisters of basal female patients with cancer of the female sex organs but not among the brothers, and among the brothers of basal male patients with cancer of the prostate but not among the sisters. A second important finding was that, in this population of sibs, cancer developed at a much earlier age (table 2).

⁸ Wassink, W. F.: *Genetica* 17:103, 1935.

⁹ Waaler, G. H. M.: *Ueber die Erbllichkeit des Krebses*, Norske Videnskaps Akademi i Oslo, 1931.

TABLE 2.—*Proportionate Cancer Mortality in Sibs of Basal Patients with Cancer, Analyzed by Age Groups (Waler)*

	Males in Age Groups					Females in Age Groups				
	40–	50–	60–	70–	80–	40–	50–	60–	70–	80–
General population	11	20	22	14	5	16	22	21	12	5
Sibs	16	42	27	18	5	49	47	35	18	5

The next step was to see whether the organ incidence in the cancerous relatives of basal patients suffering from cancer of one particular organ, e. g. the mamma, was the same as it is in the general population, which would indicate a general susceptibility to cancer of all organs, or whether it was different from that of the general population. Waaler found that in cancer of the mamma an inherited susceptibility affects mainly the female relatives (as seen in table 1) and in those female relatives mainly the "homotope organ"—the mamma (table 3).

TABLE 3.—*Percentage Cancer Incidence in Homotope and Heterotope Organs in Sisters*

	Of Basal Patients with			
	Cancer Other Than		Cancer of	
	Mamma	Uterus	Mamma	Uterus
Cancer appeared in 100 cancerous sisters in				
Mamma	16	—	45	—
Uterus	—	8	—	35

That is to say, among 100 cancerous women who had a sister afflicted with cancer of the breast—the basal patients—45 women would have cancer of the breast; while in 100 cancerous women whose sisters—the basal patients—had cancer in some organ other than the mamma, only 16 women would have cancer of the breast. This proportion (16 per cent) of breast cancer in the total organ incidence approximates that found in the general female population.

A strikingly similar result was obtained by Wassink in the Netherlands (table 4).

This table is given here because it illustrates another important point, namely the chance of a development of cancer incurred by the close relatives of basal patients with breast cancer. This is a question frequently asked by relatives of cancer patients. In Wassink's material there are 660

women as basal patients with breast cancer. Only 207 of these women had a history of cancer in other members of the family, so that as many as 453 of these basal patients had no relatives with cancer of any organ. But in the 207 basal patients with cancerous relatives the incidence in the relatives of breast cancer was remarkably high. Among the 192 cancerous female relatives more than one-half had breast cancer, namely 112 women, while in the general population of Dutch women breast cancer affects only about 10 per cent of all cancerous women.

TABLE 4.—*Incidence of Cancer of All Organs and of Breast in Relatives of Patients with Breast Cancer (Wassink)*

Number of basal patients with breast cancer.....	660 females
Number of these basal patients having relatives with cancer.....	207 females
Number of relatives with cancer of all organs.....	301
Females	192
Males	109
Number of relatives with breast cancer.....	112 females
Number of relatives with cancer of organs other than breast.....	189
Females	80
Males	109

These relationships, observed in the human subject, harmonize remarkably well with those arrived at from the experimental side. For sites such as the lip or the skin, sites exposed to agencies acting from without, the incidence of cancer is predominantly determined by the absence or presence of a carcinogenic agent coming from without—the “exogenous carcinogenic agents.” For organs not exposed to the same extent to agencies acting from without but subject to hormonal influences leading to carcinogenesis, such as the mamma and the uterus—the “endogenous carcinogens” as we may call them—the incidence of cancer is governed largely by intrinsic factors of susceptibility. For such organs as the esophagus and the stomach, which are exposed to agencies coming from without, the development of cancer depends on both factors: the presence of exogenous carcinogenic agents and the existence of an intrinsic inherited susceptibility, of which either the one or the other may predominate.

We have just seen how the incidence of cancer is affected in a population selected in such a way that the intrinsic factor of susceptibility predominates. How can we go about to select a population in which the incidence of cancer is governed by the presence of exogenous carcinogenic agents? This brings us to the next section.

Social Factors in Cancer

For organs exposed to carcinogenic agents coming from without, "exogenous carcinogens," the incidence of cancer is determined largely by the presence or absence of the exogenous carcinogens. This is clearly demonstrated by occupational cancers. Cancer of the scrotal skin is rare among the general population but relatively frequent among the chimney sweeps and among the cotton spinners in England, who are exposed to the mineral oil used for lubricating the spindles, the so-called "mule spinners' cancer." In these occupations the carcinogen induces scrotal cancer. It does so only in a fraction of the individuals exposed to the carcinogenic agent, namely in those persons with a high susceptibility to skin cancer; but even these persons would not have developed scrotal cancer if they had not engaged in those particular occupations. The occupation determines the incidence. A statistical analysis carried out nearly twenty years ago by Stevenson,¹⁰ chief medical officer to the registrar general of England, has demonstrated that this relationship extends far beyond the skin and beyond occupational cancer and applies also to the upper part of the alimentary tract. His analysis was carried out on the male population in England, which he divided into five social classes. Studying the cancer incidence for a number of separate organs, he found that in the organs exposed to exogenous carcinogens, which in addition to the skin include the alimentary tract from the mouth down to and including the stomach, the cancer incidence was highest in the lowest social class and fell with a regular diminution through the other social classes to show the lowest incidence in the highest social class. In the group of organs not exposed to agencies coming from without, a group which includes the lower alimentary tract, the incidence of cancer was approximately equal in the different social classes. These results are important both from theoretical and from practical point of view. They show as a general proposition that the etiologic factors concerned in cancer of the upper alimentary tract are different from those operative for the lower alimentary tract. Their practical importance lies in the inference that the high incidence of cancer of the upper alimentary tract is related to the mode and habits of life of the lower social classes. This relationship may be called "social cancer." I have said earlier that cancer in man is an experiment carried out by nature on man. But occupational cancer is really an experiment carried out by man in his ignorance on himself. When the study of experimental carcinogenesis demonstrated the fact that in some occupations man exposed himself to chemical substances which were carcinogenic for the skin of animals, occupational cancer

¹⁰ Stevenson, T. H. C.: Registrar General's Decennial Supplement, England and Wales, 1921; Part II, London, 1924.

became a preventable disease. Social cancer is also an experiment carried out by man in his ignorance on himself, and with increasing knowledge of the exogenous factors involved it should, like occupational cancer, become a preventable disease.

We have here another example of the value of breaking up the available data concerning human cancer into groups if we wish to obtain an insight into the remote causal factors determining the incidence of cancer in man. Previous investigations on the incidence of cancer in different social classes had failed to yield differences which statisticians considered to be significant. But when each site is considered separately a definite relationship comes to light.

Social cancer affords a clue to the nature of the etiologic factors for cancer of these sites. It even suggests the possibility of preventing the disease. If the mode and habits of life of the lower social classes could be corrected so as to bring them up to the standard of the higher classes, it is justifiable to expect that a considerable diminution in the incidence of cancer of the upper alimentary tract would result.

This would apply also to the stomach. Cancer of the stomach is responsible in most European continental countries for one-half or more of the total cancer mortality. In this country it can be estimated to kill on the average 150 persons every day of every year. It presents a problem which cannot be easily investigated in animals, because in almost all species of animals gastric cancer is very rare and it has been difficult up to now to induce it experimentally with any degree of regularity. For investigations on the etiologic factors we are, therefore, dependent at present mainly on clinical and pathologic observations on man. For such investigations the conception of the existence of precancerous conditions on the basis of which cancer develops has been particularly helpful. Before discussing the etiologic factors for cancer of the stomach in man, I shall have to consider briefly the general meaning of the precancerous condition.

Precancerous Conditions in Man

Let me recall that, when a carcinogenic agent is allowed to act on a tissue, a considerable period of time elapses before the development of a malignant condition manifests itself. During the prolonged preparatory period the tissue undergoes a pathologic change.

The conception of a precancerous condition is not new. It was first formulated many years ago by dermatologists for certain pathologic skin conditions and it was then defined as a condition in which cancer arises subsequently with a high degree of frequency. For man that definition still holds good. In human cancer it is, necessarily, a purely empirical definition and is not based on morphologic criteria, as is cancer itself. It is

easy to understand why it should have been formulated by dermatologists. For in the skin the whole process of carcinogenesis is visible to the naked eye. It was later recognized also for some other organs visible to inspection, such as the tongue or the vulva. But these examples were considered by many as pathologic curiosities and not as visible examples of a general phenomenon preceding cancer. In fact, such a generalization has been contested even in recent years—and sometimes contested with some heat—by writers who claimed to speak with authority on cancer. But since it has been demonstrated experimentally that carcinogens, to produce their effect, require a prolonged period of time during which the tissue on which they act undergoes a series of pathologic changes, and since, as explained previously, the characteristic age incidence of spontaneous cancer in man and in animals finds an explanation in this long period of induction, the existence of a precancerous condition has established itself as a fairly general phenomenon in the origin of cancer. It has encouraged clinicians and pathologists to search for such conditions in different organs.

It should be noted that the precancerous condition is not necessarily represented by an epithelial hyperplasia, as in experimental skin cancer. It may be an epithelial atrophy. There are quite a number of atrophic conditions which have been found empirically to be precancerous, such as radiation dermatitis, kraurosis vulvae and the atrophic undescended testicle. Whether an epithelial hyperplasia as such or an epithelial atrophy as such are precancerous depends on the conditions by which they were produced. In the gastric mucosa three precancerous conditions have been identified: one, a gastric polypus, is hyperplastic; the two others are atrophic in nature—a gastric ulcer and chronic atrophic gastritis.

The Origin of Cancer of the Stomach

The stomach is in man the organ most frequently affected by cancer. In this country about 30 per cent of the total recorded mortality from cancer is represented by the recorded mortality from gastric cancer. I intentionally use the expression "recorded mortality," because there is reason to believe that gastric cancer is grossly underdiagnosed and that the actual incidence of gastric cancer is much higher. I also use intentionally the terms "mortality from gastric cancer" and "incidence of gastric cancer" as synonymous in order to bring home the fact that the percentage of patients with gastric cancer that are cured by operation is depressingly low. Even in the best clinics it does not exceed from 3 to 5 per cent of all patients. These unsatisfactory results have engendered in the medical profession a pessimistic outlook on the disease. But in view of the outstanding frequency of this form of cancer it is clear that we cannot hope materially to diminish the total cancer mortality unless there is an im-

provement in the results of the treatment of gastric cancer, and there are now reasons for a less pessimistic outlook. In making this statement I do not presume to offer a personal opinion. I rely on statements made by men better qualified by personal experience to judge than I am. I refer particularly to the views expressed at the recent conference on gastric cancer organized by the National Advisory Council on Cancer in October 1940 and reported in the *Journal of the National Cancer Institute* in February 1941 and to the monograph by E. M. Livingston and G. T. Pack "End Results in the Treatment of Gastric Cancer," published in 1939.¹¹ Briefly summarized, the argument runs as follows: Gastric cancer can be cured in from 30 to 40 per cent of those cases which come to the surgeon at a stage when the disease is operable and before wide dissemination has occurred. This amounts at present to about 15 per cent of all cases of gastric cancer diagnosed as such. Gastric cancer is admittedly difficult to diagnose at this stage, and the low percentage of successful treatment is due mainly to the fact the great majority of patients—about 85 per cent—reach the surgeon at a stage at which the disease has become inoperable. On this point Livingston and Pack have this to say: "The medical practitioner, the consultant and the radiologist may play precisely as great a practical role as the expert surgeon through their influence on the most important single item, that of high operability rates." And again: "The operability rate among patients with gastric cancer may be looked upon as an index of medical efficiency in the management of the disease. The role of the medical practitioner equals or even exceeds the importance of the role of the skilled surgeon." One reason for a more hopeful outlook is the improvement in modern methods of diagnosis. A second reason is the possibility of recognizing the existence in patients of precancerous conditions. A third reason is the significance of a family history of gastric cancer. The question may be raised whether the recognition of a precancerous condition in the gastric mucosa of a person with a family history of gastric cancer should not justify immediate surgical intervention. Lastly there is the fact that carcinomas of the gastric mucosa vary greatly in their tendency to metastasis, so that some types of gastric carcinoma may reach a considerable size before they develop metastatic growths.

The importance of the pathologic conditions in the gastric mucosa which may lead to cancer raises the question of their etiology. A chronic atrophic gastritis, which is the condition most frequently preceding cancer, may be brought about by a variety of conditions. They can be summarized as chemical, mechanical or biologic insults to the gastric mucous membrane.

¹¹ See also Cooper, W. A.: The Problem of Gastric Cancer, *J. A. M. A.* 116:2125 (May 10) 1941.

An example of a biologic insult which may be an etiologic factor in gastric cancer is represented by defective oral hygiene or, in plain English, a "dirty mouth." This leads to defective mastication and to the continued swallowing of infected matter. These considerations rob the etiology of cancer of the stomach of the mystery which has been believed to surround it, and they direct attention to factors which are so frequent and familiar that they might be called banal. It is probably this group of etiologic factors which is responsible for "social cancer," i. e. the higher incidence among the lower social classes of cancer of the upper alimentary tract. In most people these insults to the gastric mucous membrane will not go beyond an atrophic gastritis or possibly an ulcer, but in individuals with an inherited susceptibility to gastric cancer they eventually induce cancer. There is so far no convincing statistical evidence that the excessive consumption of alcohol is an important factor in inducing gastric cancer, but Wassink has brought evidence that it is of etiologic significance for the pharynx and esophagus.

A Hormonal Etiology of Cancer of the Mamma and of Some Other Organs

The discovery that cancer can be induced by a number of chemical substances foreign to the physiologic economy of the body—that is to say, substances not formed by the body—has made it possible to understand the development of cancer in man in such an organ as the skin, which is exposed to agents coming from without. But how does cancer arise in organs not so exposed? A hormonal etiology of cancer of the breast was first predicated by Leo Loeb¹² twenty-three years ago. It has been demonstrated experimentally for organs, such as the mamma, the uterus and the thymus, that substances formed in the body and having hormonal functions may be carcinogenic for these organs. At first sight the fact that a hormone can induce cancer seems startling. But on consideration it solves a difficulty. That cancer can be induced in the exposed sites by the action of carcinogenic agents which play no part in the physiologic economy of the organism is easy to understand. The difficulty was to conceive how cancer can arise in organs and tissues not accessible to the action of such exogenous carcinogenic agents. The experimentally established fact that a substance formed in the body and circulating in the blood stream is carcinogenic for at least some of these unexposed organs, the mamma, the uterus, the prostate and the thymus, resolves this difficulty. But it raises at the same time a new problem. If a hormone can act as a carcinogen for a certain organ, why does not cancer develop in every individual?

¹² Loeb, Leo: J. M. Res. 40:477, 1919.

We know that the strength of the carcinogenic agent—in this case the estrogenic hormone—is one factor. Observations on different strains of mice give no evidence that the females of the high cancer strains secrete more estrogen than those of low cancer strains. But the estrogenic hormone of the ovary is functionally integrated with the hormones of the other endocrine organs.¹³ Some of these act synergistically, e. g. a hormone from the adrenal cortex, others antagonistically, e. g. a hormone from the anterior pituitary. As a result of this endocrine integration, alterations in the functional activity of some endocrine organs other than the ovary may lead to an endocrine imbalance either in the direction of reinforcing the action of the estrogen or in the opposite direction of antagonizing it. In the maintenance of this endocrine balance for the female sex hormone the pituitary gland and the adrenal glands take a leading part. Adrenalectomy makes the animals resistant to the effect of the estrogenic hormone.¹⁴ Ovariectomy, if performed at birth, leads after a long time interval to a nodular hyperplasia of the adrenal cortex in strains of mice with a high incidence of spontaneous breast cancer but not in low cancer strains. The adrenocortical hyperplasia is followed by development of the mamma which may proceed to cancer.¹⁵ A remarkable feature of this phenomenon is that it applies also to male animals, in which castration soon after birth may lead to a nodular hyperplasia of the adrenal cortex and even to mammary cancer.¹⁶ It is conceivable, then, that a disturbance of the endocrine balance in a direction enhancing the functional activity of the estrogenic hormone, such as an adrenal cortical adenoma, may be an etiologic factor for breast cancer. The association of such changes in the adrenals with spontaneous mammary cancer in animals has been recorded by Bagg¹⁷ in rats and by Greene¹⁸ in rabbits. Instead of a cortical hyperplasia, a degeneration of the adrenal medulla has been found to be associated in some strains with a high incidence of breast cancer.

Comment

This is only a brief outline of the various etiologic factors concerned in breast cancer. But it is sufficient to show that a new field for clinical and pathologic observations has been opened. The presence of a family history of breast cancer is an extremely valuable aid in the early diagnosis, espe-

¹³ A detailed discussion of these relationships may be found in Cramer, William: *The Sex Hormones and the Endocrine Balance*, Middleton Goldsmith Lecture, Bull. New York Acad. Med. 17:3, 1941.

¹⁴ Cramer, William, and Horning, E. S.: *Lancet* 1:192, 1939.

¹⁵ Woolley, G.; Fekete, E., and Little, C. C.: *Proc. Soc. Exper. Biol. & Med.* 45:796, 1940.

¹⁶ Woolley, G.; Fekete, E., and Little, C. C.: *Endocrinology* 28:341, 1941.

¹⁷ Bagg, H. J., and Hagopian, F.: *Am. J. Cancer* 35:175, 1939.

¹⁸ Greene, H. S. N.: *J. Exper. Med.* 70:147, 1939.

cially when the clinical or pathologic evidence is doubtful. Another problem of practical importance requiring solution is the question whether patients with breast cancer and a family history of breast cancer are more likely to develop a second primary tumor in the other breast. Further, a thorough examination of the adrenals and the pituitaries at autopsies of patients dead of breast cancer and with a family history of breast cancer may reveal a group in which there is an association between breast cancer and abnormalities of these endocrines.

Conclusion

I began this lecture by asking the question Why does a patient get cancer? We have been told often enough, even in recent times, that this question cannot be answered until the problem has been solved of the nature of the proximate cause of cancer—that is, the nature of the intracellular changes by which a normal cell is transformed into a cancer cell. This belief engenders a pessimism which hinders further progress. The point I have tried to make in this lecture is that there is no longer a central problem of cancer on the solution of which further progress depends. In fact, it is an error to think in terms of a central problem of cancer. From a correlation of the results obtained by the study of experimental carcinogenesis in animals with clinical and pathologic observations and with statistical investigations on cancer in man, it has become evident that there is a multiplicity of etiologic factors and that the etiology of cancer in man, as in animals, has to be considered as a separate problem for each organ.

In this way we are now beginning to trace cancer in man down to its various sources of origin. What is more, we are entitled now to consider the possibility of preventing several forms of cancer in man by attacking the disease at its origin instead of remaining on the defensive until the disease has attacked man. Further progress along these lines is possible by the same collaboration of the laboratory worker with those concerned with the study of cancer in man, which forty years ago established the curability of cancer in its early stage.

Shortage of Microscopes

It is highly probable that during the next few years students will not be able to purchase new microscopes. Alumni, who have no need for their microscopes, can help in a solution of this problem. Mr. James J. Ritterskamp, Purchasing Agent of the University, will be pleased to hear from alumni and arrange to purchase used modern microscopes.

Ageing of the Reproductive System

WILLARD ALLEN, M.D.¹

The organs of reproduction illustrate better than any other the interrelation between the endocrine glands and the processes of growth and decline. Throughout the individual's entire life, from the earliest days of intrauterine existence to death, the uterus and vagina respond to the sex hormones by altered patterns of growth.

Prior to birth it is probable that the structures of Müllerian origin owe their normal development in part to the action of estrogens (and possibly androgens and progesterone) produced by the placenta of the mother. At any rate, the vaginal epithelium of the new born child is thick, contains glycogen and is histologically similar to the vaginal epithelium of the mother. As soon as delivery occurs the child, as well as the mother, is deprived of this stimulus, and as a result the vaginal epithelium desquamates. Two weeks after delivery, the vaginal mucosa of both the mother and the child is well involuted, and in some instances this is accompanied by uterine bleeding. This has actually been shown to be accompanied by breakdown of the endometrium similar to that which occurs at the time of menstruation.

The reproductive organs of the unborn fetus of both sexes also can be altered by the administration of the sex hormones to the expectant mother. In rats, estrogens interfere with the normal development of the organs of reproduction in the male, and hypospadias results. The unborn females are apparently not adversely affected by hyperestrinism. Androgens do not adversely affect the males but seriously interfere with the canalization of the vagina and they also stimulate the rudimentary male accessories.

I have cited these effects of estrogens and androgens only to indicate that even before birth the accessory organs of reproduction respond to stimulation by hormones which are known to be acting in the mature individual. As a corollary it is of interest to speculate upon the cause of certain developmental defects which are occasionally encountered. Male pseudohermaphroditism is a good example. In this condition the gonads are testicular but the accessory organs of reproduction show varying degrees of feminization. Usually there is a rudimentary vagina and a hypospadiac penis, a condition not unlike that produced in male rats subjected to hyperestrinism prior to birth. In other instances the vagina may be normal, the penis represented only by a normal female clitoris, and there may be no uterus.

¹ Professor of Obstetrics and Gynecology, Washington University School of Medicine. Presented at the third annual meeting of the Club for Research on Ageing, Baltimore, Md., March, 1942.

In such cases the breasts, bodily stature and emotional makeup are entirely feminine even though the gonads are still testicular. This condition is known to be hereditary—in some families at least. If this feminization of genetic males is due to hyperestrinism prior to birth, it may be due to an abnormality of the placenta which results in overproduction of estrogen very early in gestation. Another equally plausible explanation, however, is that the accessory organs are more susceptible to estrogen than normally and that this increased susceptibility is hereditary.

Following birth the reproductive organs obviously have to carry on without the benefit of any help from the mother. As I have already mentioned, the uterus and vagina involute as soon as the child is separated from the mother. They grow slowly through childhood under normal circumstances. However, puberty can be ushered in by administration of estrogens at almost any age prior to the usual time. Tumors occasionally arise in the ovaries which produce estrogens (and possibly progesterone), and under these circumstances the breasts develop, pubic and axillary hair appear and the body as a whole assumes the mature feminine habitus. Clinically also estrogens have been given to produce a thickened vaginal epithelium in order to eradicate gonococcal vaginal infection, and when given hypodermically in adequate amounts signs of precocious puberty have been noted. There is every reason to believe, therefore, that in the female there is a relatively asexual period in childhood during which the organs of reproduction are comparatively quiescent. Furthermore, failure of growth of the uterus and vagina can not be attributed to immaturity and inability to respond, since they do respond when estrogens are given. It might be stated parenthetically that these observations recorded for the human are entirely in accord with extensive experiments in the common laboratory animals.

Precocious puberty likewise occurs in rare instances when no tumors of the ovaries are found. These are doubtless due to the early awakening of the ovaries brought about by stimulation from the anterior pituitary. Early maturity of this sort has been observed occasionally after meningitis without there being any evidence of a pituitary tumor. This type of precocious puberty is accompanied by development of the ovary such as occurs normally many years later. The ovarian activity may be sufficiently orderly to result in ovulation. Pregnancy can occur and has occurred, witness the Peruvian child of six who became pregnant and was delivered of a normal child. This obviously could not occur in those cases of precocious puberty due to ovarian tumors. Why irritation at the base of the brain, such as occurs from meningitis, should cause the anterior pituitary to begin secreting amounts of gonadotropic hormones (and others, too) sufficient to produce precocious

puberty is not clear. This experiment of Nature, however, illustrates clearly that the immature ovary is capable of behaving in the manner characteristic of the adult many years before it normally should, provided the proper stimulus comes along. Under normal circumstances we have to assume, therefore, that when the appointed time arrives the child begins to mature because the pituitary begins to increase its output of gonadotropic hormones. Why it does not do this prior to the normal time is a mystery. It is just another example of the process of growth which proceeds inevitably and in such an orderly manner. As Stockard so aptly says, "One can only say in general that these changes result from a biologically harmonious state which develops with time."

Adolescence marks the next period when the sex hormones begin to affect markedly the female individual. In many instances maturation occurs in a relatively short period of time. The child may mature into a woman almost overnight. Regular menstrual periods are established, and the child is no longer a child but in reality a woman capable of bearing children. In other instances, and in fact generally, adolescence occupies a period of several years, and only after a period of transition do menstrual cycles become regular and does ovulation occur regularly. During this transitional period endocrine imbalance is common. Many adolescent girls have a few menstrual periods and then develop amenorrhea and obesity, conditions which later on spontaneously disappear. Others have irregular menses interspersed with periods of long continued uterine bleeding. These individuals have temporarily lost their ability for cyclic ovarian activity. Here again the disturbance, really one of failure of ovulation, is often transitory, but occasionally the condition is so persistent as to cause serious anemia. Several types of treatment have been found beneficial, but in general any remedy which disturbs the existing endocrine balance may interrupt the bleeding and restore the ovary to cyclic activity. For example, thyroid, estrogens, progesterone, testosterone and gonadotropins have all been found helpful.

There are many different manifestations of ovarian dysfunction occurring during adolescence, but in the majority of girls, after a few years, the individual stabilizes and has normal cycles. There are a few, however, who always show evidence of abnormal ovarian behavior. Some individuals develop apparently normally, have fully developed reproductive organs, yet have no menstrual periods and are sterile. Others have recurring episodes of abnormal bleeding and are also sterile. Nothing as yet has been found which permanently restores them to normal ovulatory cycles. One has only to recall, however, that at least one strain of rats has been produced by inbreeding in which ovarian dysfunction, manifested usually by failure of ovulation, occurs regularly. The animals are smaller, fertility is lower and

they have a higher incidence of carcinoma of the breast than normal rats.

There is one other aspect of these disturbances seen during adolescence and in young women. Many of them are amenable to thyroid medication. In general those that respond promptly to desiccated thyroid have normal, fertile cycles as long as thyroid is taken, only to relapse soon after discontinuing thyroid. In individuals who are improved by thyroid, is the thyroid at fault or is the pituitary unable to produce an adequate amount of thyrotropic hormone? It is obvious that the condition is not one of complete thyroid failure from birth because they are not cretins. One can only say that it has been found empirically that thyroid is beneficial. These persons may also be persons whose genetic makeup is defective.

When the young woman has safely passed through adolescence and has begun to have regular cycles, disturbances of ovarian function are not so common and in general disturbances do not recur until the period of decline begins. There may be upsets, however. For example, the young woman who travels from one part of the earth to another part, or even from one part of the country to another, may develop amenorrhea or functional bleeding. These upsets are frequently accompanied by hypothyroidism, a fact which suggests that a change in dietary habit may be the underlying cause.

The period of decline is, of course, most significant in so far as ageing is concerned. Women often feel that the climacteric is the end, but it is far from that. Life and good health can be enjoyed for many years after the menopause. In fact, the woman who lives to reach 80 has as many years of reproductive inactivity as she has of reproductive activity. Simple reiteration of this obvious but often forgotten fact helps the climacteric woman to face the future with greater equanimity. Lack of emotional strain is of great help, and this obviously is aided by pleasant home surroundings and a marriage which has already been a long and happy one. The unmarried, or otherwise sexually maladjusted woman frequently has a great deal of difficulty for several years, whereas the woman happily married may go through the climacteric with little if any discomfort.

The menopause, or climacteric, is not an abrupt change. Just as adolescence is a period of gradual growth and maturation, so the climacteric is a period of gradual decline. The ovary probably reaches its maximum peak of activity at about 30. At least the incidence of twinning, which 80 per cent of the time is due to multiple ovulation and hence is evidence of maximum ovarian activity, reaches its maximum at about 30. The majority of women do not have any of the classical symptoms of the climacteric until after 40. From that age to 50 the symptoms of decline begin to appear, but it is not uncommon for the cessation of menses to be delayed until after 50 or even 55.

For a period of several years, decrease in ovarian activity is accompanied by more or less characteristic symptoms. Even while the cycles are still regular there may be a change in the duration and type of menstrual bleeding. There may be headaches and hot flushes, occurring only during the menstrual period. Physicians interested in the menopause are now beginning to realize that many of the ill defined disturbances which precede the frank menopause are due to decreasing ovarian activity. Finally, after a variable period of time, the flushes increase in number and in general the headache and depression lessen. Then, after another period of variable duration, the flushes disappear and the menopause can be considered finished.

The climacteric is most certainly brought about by ovarian deficiency. It can be precipitated at any age after puberty by surgical removal of the ovaries or by destruction of the ovaries from any cause, such as x-radiation, radium, infectious processes or tumors. The symptoms appear usually within a month. The uterus gradually decreases in size, the breasts atrophy and the vaginal epithelium becomes thin and contains little glycogen. The retrogressive changes can be prevented by the administration of estrogens, or even though retrogression is advanced, the organs can be restored approximately to their normal state by estrogens. At the same time the subjective symptoms, such as nervous instability, headaches, indigestion, and so on, are alleviated. All clinical experience points in one direction, the symptoms and signs of ovarian deficiency can be alleviated by the use of adequate amounts of estrogenic hormone. It is not surprising that estrogens relieve the symptoms of ovarian deficiency. A clearer example of endocrine deficiency could not be expected. The intriguing part of the climacteric is this: The woman who has passed the normal climacteric reaches a stage when practically no estrogens are being produced, having no symptoms and enjoying good health. The younger woman who has an artificial menopause may have troublesome symptoms for 15 years or more, even though she also has reached a stage of fairly complete estrogenic deficiency. Why in one case do the symptoms persist for years and in the other case do they disappear? There is much yet to be learned about the effects of estrogenic (or ovarian) deficiency. The question naturally arises, "Should persons with symptoms arising because of gradually failing ovarian activity be given estrogen?" Here is a patient, often miserable, and the physician has a specific remedy, yet the patient is experiencing a normal sort of misery. One of the duties of the physician is to relieve pain and discomfort wherever possible. In obstetrics, for example, alleviation of pain is of great help, yet if the use of pain-relieving drugs merely delayed the appearance of pain, the obstetrician would most certainly take the attitude

that the drugs should not be used. There are, of course, well recognized instances when drugs of this sort should not be used so that labor will progress entirely naturally. In like manner, if utilization of estrogens merely puts off the evil day and the symptoms would have to be experienced eventually, it might be wiser not to give estrogens to the woman experiencing the menopause at the usual time. Fortunately, the question usually does not have to be answered. There is a great deal of fashion in the practice of medicine. The patient frequently specifies the treatment and then, of course, estrogens are given. Women nowadays are led to believe that ageing can be made a pleasant process, simply by the faithful use of the waters of the fountain of youth.

The young woman, unfortunate enough to be deprived of her ovarian function, soon becomes a physical wreck in many instances. Detailed observation of such patients before, during and after therapy is a revelation in itself. When adequate amounts of estrogen are used the change is amazing. Young women require larger amounts of estrogen, compared to older women. Some require 2 or 3 mgm. of estradiol benzoate weekly, whereas older women get relief from 0.2 to 0.5 mgm. per week. Some skeptics insist that equally good results can be obtained by the use of hypodermics of saline or sesame oil. That has not been my experience. I have seen patients who could correctly tell whether they were getting .3 mgm. or 1.3 mgm. of estradiol benzoate, and it is common observation that decreasing the dose, even though the amount of solution injected is the same, is accompanied by increasing symptoms. Even a woman of 70 can be rejuvenated by estrogens to the point where bleeding from the uterus will occur on withdrawal of the medication.

Having now probably exhausted you with this account of the rejuvenation of castrated or elderly women, it perhaps may be appropriate to pause and ask if the rejuvenation is anything more than rejuvenation of the organs of reproduction (excluding, of course, the ovaries). I think there can be no doubt about the mental uplift which occurs. It has also been my impression that young women who have been deprived of adequate ovarian function for some time look prematurely old, and that such women look different after several months of estrogen therapy. I have not as yet had the opportunity of giving estrogens for a considerable period of time to a person of 60. That type of experiment is one which would probably require self medication. The real question, of course, is, what would happen if estrogens were given continuously from the beginning of the menopause throughout the remaining years of life?

Since we are all interested in old age, the question might properly be asked, "Would prolongation of the sexual life by use of estrogens shorten

or prolong life, and would it make the shortened or lengthened life more worthwhile and pleasant?" As yet we have no answer to this question.

I think there can be no question about the desirability of conserving full ovarian function as long as possible. Partial destruction of ovarian function likewise leads to many disturbances in ovarian function.

It is an old observation that removal of one ovary causes the remaining ovary to assume the duties of both. In those mammals that have several young in the litter, removal of one ovary does not materially decrease the size of the litter. Whereas prior to unilateral oophorectomy each ovary may have shed five eggs at each estrous period, after operation the remaining ovary discharges ten eggs each time. Whether or not this type of ovarian deprivation leads to premature ovarian failure, I cannot say. It is common knowledge, however, that removal of one ovary in young women is followed by a premature menopause. In general, it might be stated with some accuracy that removal of one ovary shortens the remaining reproductive years by one-half. Hemicastration, however, does not usually seriously alter the ability to conceive. There are many women who have had several children of both sexes following removal of one ovary.

The statement is frequently made that removal of one ovary does not disturb the menstrual cycle. This is incorrect. I have seen several young women who had one ovary removed and have presented the same history. For two to three years the cycles were regular then the interval decreased from 28-30 days to 21-25 days. Then some of the menstrual periods became abnormal—usually the flow became excessive and prolonged. Often there was spotting for several days before the normal flow began. The remaining ovary hypertrophied and became painful. Repeated examination of such patients shows the ovary to vary markedly in size from time to time. This means just one thing. Some of the time ovulation has not occurred and a follicular cyst, possibly a luteinized one, has appeared. This probably indicates improper stimulation by the anterior pituitary.

Removal of one ovary and resection of the remaining ovary, as might be expected, causes a more serious disturbance. Lipschütz, many years ago, showed in guinea pigs that this disrupts the mechanism of ovulation and leads to the formation of follicular cysts. In guinea pigs and rats a state of more or less persistent estrus results. This operation used to be done frequently in young women who had chronic salpingitis produced by gonorrhea. The results were very bad, chiefly because the menstrual cycles soon became very abnormal. Cycles are irregular, and continuous bleeding is often very troublesome.

The disturbances of ovarian function which follow partial removal of the ovaries are similar to those which occur normally at the climacteric. I have

the general impression, however, that disturbances of the cycle occurring as a result of partial destruction of the ovaries may persist longer and be more troublesome than disturbances occurring at the normal climacteric.

There is at least one other means of altering gonadal function, and that is by malnutrition. It is common knowledge that inadequate food intake may seriously disturb gonadal function. For example, a simple reduction of the food intake of normal guinea pigs to one-third of the normal level for only two weeks results in atrophy of the ovaries and thyroid as marked as that which follows hypophysectomy. This decline of the ovaries and thyroid is apparently due to pituitary failure, since administration of thyreotropic hormone causes hyperplasia of the thyroid and interstitial cell stimulation of the gonad. It would seem, therefore, that the anterior pituitary goes into low gear when the food intake is inadequate. This, of course, can be interpreted as a defense mechanism. Similar pituitary deficiency, so-called pituitary cachexia, is occasionally seen in women, suffering from anorexia nervosa. This is a condition in which for some reason, usually psychic, the patient cannot or will not eat. After a variable period of time there are, in addition to the obvious loss of weight, signs of fairly complete endocrine failure manifested in so far as the reproductive organs are concerned by amenorrhea and atrophy of the uterus, tubes, ovaries, vagina and breasts.

There is still another way of disrupting ovarian activity,—simple removal of the uterus. Unfortunately, it is not possible to fully harmonize all of the observations that have been made. In the rabbit, removal of the uterus at a time when there are functioning corpora lutea in the ovaries prevents the retrogression of the corpora. In the normal non-pregnant animal the corpora lutea remain functional for about two weeks, whereas following hysterectomy they remain functional for two months. In the rat, however, estrous cycles recur perfectly normally after hysterectomy. The same is true for the monkey. In women, however, even in young women, it is not infrequent to have menopausal symptoms appear two or three years after hysterectomy. Only two weeks ago, I saw a woman of 28 who was already having menopausal symptoms, including moderate atrophy of the vaginal epithelium, only two years after a complete hysterectomy.

I have cited these various means of producing ovarian deficiency only to emphasize once more that it behooves every physician, especially the operative gynecologist, to spare no effort in attempting to conserve not just some ovarian tissue, but all ovarian tissue as long as possible. Every effort should also be made to keep the state of general health as good as possible. In this connection it might also be well to start a campaign to encourage young women to marry and have children while they are still young, rather

than to defer marriage until financial security is achieved, the passions lost and married life platonic rather than torrid. The childless woman is in general subject proportionally to more gynecological troubles than the woman with children.

I have made no mention thus far of the effects of castration or ovarian decline on the endocrine glands. This can be discussed better by others. Suffice it to say that after castration the anterior pituitary contains more follicle stimulating hormone and secretes more, since there is more in the blood and urine. This increase is apparently a direct result of estrogenic deficiency, since injection of estrogens prevents the increase.

The ever present question of carcinoma as a factor in ageing and the relation of the sex hormones to carcinoma is always before us. There are a few salient points which should be remembered. Carcinoma of the breast and of the uterus is exceedingly common. A substantial part of gynecology deals with carcinoma.

Carcinoma of the cervix is very common and it occurs at all ages from 20 to the grave. We have had in adjoining beds on the ward young women of 22 or 23 who have never had children and women of 70 with carcinoma of the cervix. This is worth remembering when some hormone enthusiast says that carcinoma of the cervix is due to too much estrogen. Furthermore, there is no evidence of rejuvenation of the vaginal epithelium in patients developing carcinoma of the cervix after the menopause, yet if estrogen were given to them the vaginal mucosa would respond in the usual manner. The statement is also made that carcinoma of the cervix occurs only rarely in Jewish women, but I know of no reason for believing that estrogen is different in Jewesses and Aryans. The statement is also made that multiparity is a contributing factor, but that likewise is probably of little consequence.

One can not be quite so positive regarding carcinoma arising in the body of the uterus. This disease usually begins after the menopause, but some observers think that it occurs more frequently in women who have had a late menopause. In fact, it may be a part of a late menopause. It does seem to be more frequent in women who have not borne children. Brewer has shown, however, after careful study of many cases, that when it occurs before the menopause there is no manifest disturbance of ovarian function. In fact, the endometrium, in areas not involved by tumor, responds to the sex hormones in a normal manner, and further, the cycle itself appears to be normal.

The relation of the estrogens to carcinoma of the breast in women is also not clear. Carcinoma occurs after the menopause, but most of it occurs before cessation of ovarian activity. Furthermore, the condition known as

chronic mastitis, a disorder predisposing slightly to carcinoma of the breast, is probably due to disturbed ovarian function. I believe it is also true that carcinoma of the breast is more common in women who have not borne children. In this connection it is of interest that Wolfe has developed a strain of rats in which ovarian dysfunction, manifested chiefly by persistent estrus and abnormality in ovulation, is correlated with a high incidence of carcinoma of the breast. The rats are subnormal in other ways, and the type of disturbance is similar to that seen in old rats.

This brings up the question of estrogens as carcinogenic agents. There is no question, of course, but that estrogens lead to the premature appearance of carcinoma in the breast of animals genetically disposed to cancer. In so far as this type of experiment is concerned, estrogens are carcinogenic. The interpretation is more complicated. The continuous use of estrogens severely damages the animals. The pituitary hypertrophies, the gonads are depressed, the bone marrow is altered, and growth decreases and stops. In short, the animals are perhaps so severely disturbed by the treatment that they are aged prematurely. Another factor should also be mentioned. In the normal individual the estrogens are being periodically opposed by the corpus luteum hormone, progesterone.

It probably is not necessary to summarize this discourse further than to reiterate that the woman's entire reproductive system, its growth and decline, some of the diseases which affect it, and her whole being are inseparably connected with the endocrine glands. Also, I presume you will correctly deduce that I think the woman should "select" ancestors free of cancer, with good reproductive behavior, select a good husband, raise a family and avoid meddlesome gynecologists, if she wishes to enjoy health and happiness and to say with the deluded poet, "Grow old along with me, the best is yet to be."

Fatal Poisoning from Potassium Thiocyanate Treatment of Hypertension.

W. O. Russell and W. C. Stahl: *J. A. M. A.*, 119: 1177-1181, 1942.

The thiocyanate treatment of hypertension is not free from complications which may even be fatal. In rare instances the dose of thiocyanate usually prescribed and regarded as safe for the treatment of hypertension produces a fatal intoxication, as shown by six cases collected in this study. In patients showing such an extraordinary toxicity from thiocyanate, a blood cyanate level of from 15 to 20 mg. per hundred cubic centimeters should be regarded as critical.

***Buy War Stamps and Bonds
Then Contribute to Alumni Fund***

Therapy of the St. Louis Children's Hospital

II. Treatment of Severe Diarrhea in Infants and Children

ALEXIS F. HARTMANN, M.D., '21

Aside from prophylaxis, which will not be discussed here, the treatment of severe diarrhea generally calls for: (1) prompt relief of acidosis, dehydration and anhydremia; (2) attempts to eradicate causative organisms from the gastro-intestinal tract or elsewhere by *chemotherapy*; (3) placement of the gastro-intestinal tract at rest for as long a time as seems desirable; (4) parenteral feeding, which should be as complete as possible and (5) proper methods of resumption of enteral feeding.

The theory and practice of prompt and effective relief of acidosis and dehydration have been frequently discussed (1, 2) and were considered in sufficient detail lately in this journal (3) to justify only a very brief review of our present methods in this article. The following outline should suffice:

1. Immediate administration, intravenously if possible, otherwise subcutaneously, of isotonic (1/6 molar) sodium lactate in an amount approximating 30 c. c. per kilogram body weight. This step leads to prompt dilution of the blood, which is often extremely concentrated, and to increase in plasma volume and blood flow. Improvement of circulation frequently is manifested during the fluid administration by appearance of veins which previously had been invisible, change of skin color from ashen-gray to the usual pink, increase in blood pressure in the extremities, improvement in the quality of the pulse and enlargement of the heart, which during anhydremia, is often extraordinarily small. The latter change can best be appreciated by fluoroscopy. This first step also starts the relief of acidosis, independently of renal activity. Sodium released by the conversion of the lactate into liver glycogen and by its oxidation equals about one-fourth that normally bound by bicarbonate.

2. Complete relief of acidosis. In cases known or judged to be very severe (CO_2 content of 25 volumes per cent or less), 60 c. c. more of 1/6 molar sodium lactate per kg. body weight are added to two-thirds that volume (40 c. c. per kg.) of hypotonic Ringer's solution, and the mixture¹ is then given subcutaneously and/or intraperitoneally. In the most extreme cases 30 c. c. per kg. more of the isotonic sodium lactate may be required. In

¹ This mixture is usually referred to as "fortified" lactate-Ringer's solution.

cases of only moderate acidosis, such as may be expected to accompany the usual case of acute bacillary dysentery, a half dose (30 c. c. per kg.) of 1/6 molar sodium lactate added to 40 c. c. per kg. of Ringer's solution suffices.

This second step generally also relieves dehydration completely and restores more or less completely extra-cellular fluid electrolyte loss. The quantity of lactate administered is sufficient to abolish ketosis quite promptly if the latter exists (as it usually does in acute bacillary dysentery), and probably leads to some storage of liver glycogen. The total fluid volume administered is also usually sufficient to permit diuresis, which should be expected unless plasma protein deficiency exists and leads to edema and oliguria.

3. Transfusion of whole citrated blood to provide a normal red blood cell count and satisfactory plasma protein concentration (usually 20 c. c. per kg. repeated once or twice). Plasma in any of its commercially available states may be substituted for whole blood to insure proper plasma protein concentrations, but should be considered inferior to whole blood at this stage.

Chemotherapy is employed at present as follows: As soon as acidosis and dehydration have been relieved and a good urinary secretion reestablished, *sulfadiazine* is administered orally in an initial dose of 0.1 gm. per kg. body weight and continued at 4-6 hour intervals in a total 24 hour dosage of 0.2 gm. per kg. body weight. Simultaneously succinyl sulfathiazole (sulfasuxidine) is administered in a total 24 hour dosage of 0.25 gm. per kg. body weight.

The rationale of the use of *sulfadiazine* lies partly in the fact that it possesses a definite bacteriostatic effect on at least some strains of dysentery bacilli but more largely on the fact that severe diarrhea in infants may both be initiated and complicated by parenteral infection, especially in the upper respiratory tract. Some of our worst cases of otitis media and mastoiditis have been seen in such infants, and parenteral infection is much more likely to be the cause of death than is enteral infection. Succinyl sulfathiazole is included largely for clinical observation. It is known (4) to inhibit growth of colon bacilli low in the intestinal tract and it is hoped that it may also inhibit the growth of dysentery bacilli at a low level in the intestine, and in general depress bacterial growth in the colon. In vitro studies made by Dr. David Goldring and Miss Anne M. Perley of the Department of Pediatrics on the inhibition of growth of strains of Shiga and Flexner bacilli by different sulfonamide drugs, indicate that sulfathiazole is as effectual or slightly more so than *sulfadiazine*. We prefer *sulfadiazine*, however, because of the greater protection it affords to the central nervous system (5). Such chemotherapy should be continued for about six

days, after which sulfadiazine may be continued as much longer as any remaining parenteral infection justifies.

During the period required for correction of the acid-base and water balance and the initiation of chemotherapy, the gastro-intestinal tract is put at rest by completely restricting food. Water or buffer water² is allowed ad libitum, and used as a vehicle for the administration of the sulfonamide drugs which generally are given by teaspoon or medicine-dropper as a thick suspension of the finely crushed tablets, followed by water. Restriction of enteral feeding should be continued until the clinical picture is that of significantly reduced toxemia, cessation of vomiting, and at least some improvement of diarrhea. In the majority of instances this period lasts for about 24 hours, but occasionally may require 72 hours or longer. Previously well nourished infants stand such periods of food restriction quite well, but athreptic ones must have starvation minimized by parenteral feeding, which may be begun as soon as the acidosis and dehydration have been corrected. For this purpose a mixture of equal parts of 10 per cent dextrose, 10 per cent Amigen,³ and lactate-Ringer's solution is made and given by a combination of the intravenous and subcutaneous routes. With just this mixture given in amounts sufficient to prevent recurrence of dehydration, recurrence of acidosis and ketosis may be prevented, and body protein consumption greatly minimized.

In addition, especially in protracted cases, more blood may be administered from time to time as whole citrated blood and a special nutritive plasma obtained by bleeding donors six hours after a meal rich in butter-fat and fat-soluble vitamins. In the plasma separated from such blood, may be incorporated all the known vitamins. This will be a subject reported on in detail later by Dr. Harry Lawler and myself.

When it is judged safe to resume enteral feedings, they are begun as a mixture of equal parts of 10 per cent carbohydrate (dextrose, dextrimaltose, or karo syrup), 10 per cent Amigen and buffer water (for young infants) or plain water for the older infants. This mixture is offered in gradually increasing amounts every two hours, and usually on the second or third day is alternated with small amounts of an acid evaporated milk formula⁴ in the case of the young infant, or boiled skimmed or skimmed evaporated milk in the older infant or child. If clinical improvement continues, the formula is gradually increased in amount and strengthened

² One per cent lactic acid and one-half per cent sodium-lactate sweetened with a little sugar.

³ A sterile solution of pH 6.5 containing all essential amino acids supplied by Mead-Johnson and Co.

⁴ Equal parts of evaporated milk, one percent lactic acid—15 per cent carbohydrate, and sterile water.

until it corresponds to the normal one employed for the age of the child. Solid food without residue is then added and gradually the normal diet is resumed.

Bibliography

1. Hartmann, A. F.; Perley, Anne M.; Basman, Jack; Nelson, Martha V.; Asher, Cecile; with technical assistance of Marie Morton: Further observations on the metabolism and the clinical uses of sodium lactate. *Jour. of Ped.*, 10:5, Nov., 1938.
2. Hartmann, Alexis F., Acidosis, Alkalosis and Ketosis. *Brennemann's Practice of Pediatrics*, Vol. I, Ch. 24.
3. Hartmann, A. F. Comments on some common pediatric procedures. *Wash. U. Med. Alumni Quarterly*, Vol. I, No. 2, Jan., 1938.
4. Poth, Knotts, Lee and Innue *Arch. Surg.* 44:187, February, 1942.
5. Hartmann, Alexis F.; Wolff, Dorothy; Love, Frances M.; Kendall, Barbara S.: Diagnosis and management of severe infections in infants and children: A review of experiences since the introduction of sulfonamide therapy. II. Hemolytic streptococcal meningitis. *Jour. of Ped.*, (In Press).

The Effect of Pregnancy upon Experimental Tuberculosis in Rabbits. Leo J. Wade; *American Review of Tuberculosis*, 56: 93-100, 1942.

The average duration of life following tuberculous infection in rabbits undergoing from one to three pregnancies was longer than that of tuberculous rabbits which did not become pregnant, but statistical analysis indicates that the difference is too small to be significant.

The average extent of the disease at death was less in the pregnant animals than in the control animals. Again, statistical analysis reveals that the difference is too small to be significant.

Pregnancy in tuberculous animals was not accompanied by any changes in sensitization to tuberculin but following the termination of pregnancy there was a transient decrease in the intensity of the skin reaction to tuberculin.

The appearance of complement fixing antibodies for the tubercle bacillus was retarded in those infected animals that became pregnant, but following the termination of pregnancy the titres rose to the level of those in the control group.

The Effect of Sympathectomy on Renal Blood Flow in Essential Hypertension. Thomas Findley, Etta Clinton and Joseph C. Edwards: *Surgery*, 12: 64-67, 1942.

The authors did clearance studies before and after sympathectomy for essential hypertension. They found that irrespective of the relief obtained from operation, there were no important changes in renal blood flow.

School of Medicine

REPORT OF THE DEAN

For the Year Ending June 30, 1942

To the Chancellor of the University

Sir:

I have the honor to submit the annual report of the activities of the School of Medicine for the academic year 1941-42.

During these fateful years the major problems for medical education, as for every other enterprise, have been created by world events that take precedence over all policies and programs. The main task of this Medical School during the period under review has therefore been to learn what the new requirements of medical education are, and to try to find ways to meet them with the least disruption of the primary aims and functions of an academic institution. Neither task has been accomplished, although progress is being made.

In one respect medical education in war-time has an almost unique advantage over that of most other fields of education—an advantage that aids in charting its course during the present National emergency. The advantage comes from the fact that the functions of medicine are substantially the same—and at least as valuable—in war as in peace: the prevention and cure of disease, repair of injury, relief of suffering and saving of life—with constant search for new knowledge and better methods to achieve these ends. Appreciation of the unchanging necessity for these services will insure a growing stream of recruits and protection of facilities and staffs of medical schools, where alone the recruits can be trained.

The Accelerated Program

Until the spring of 1940, members of the faculty, like other citizens, paid too little attention to the signs of the approaching storm and were fully occupied with teaching and research, with plans for strengthening and expanding staffs and facilities of the school for better performance of its normal functions.

In April 1940 Surgeon General Magee of the Army requested the Medical School to form from members of the faculty a unit for General Hospital No. 21, to become the successor to Base Hospital No. 21, the service of which in France during the First World War is one of the fine traditions of Washington University. The request was promptly accepted; and the organization of this Army Hospital Unit, among the first later called to active duty, marked the beginning of the School's preparation for the war.

At about the same time, there was an increased interest and larger enrollment of students in the Medical R. O. T. C., under the direction of Lt. Col. E. H. Perry, M.C. whose duties have since become much expanded.

Following the enactment of the Selective Training and Service Act, students, younger faculty members and employees registered on October 16, in anticipation of military duty. Many members of the faculty began to add to their duties service as physicians on Selective Service Boards, a few to Committee of the National Research Council and others undertook new research projects related to the Preparedness Program.

By the Selective Service law all students were granted occupational deferment until July, 1941, but beyond that date there was uncertainty. The policy of Local Boards lacked uniformity concerning the continuance of deferment of medical students; and there was no assurance that pre-medical students accepted for admission to the class for September, 1941 would be deferred for medical study.

By the spring of 1941, the Surgeon Generals of the Army and Navy as well as the Director of Selective Service came to realize the impending shortage of physicians and the consequent need for maintaining a stream of medical and of other technical personnel under training. Directions were issued to Local Boards advocating occupational deferment for medical and other students, and plans were authorized for granting temporary commissions to medical students in the upper classes. These procedures saved from immediate induction nearly all medical students for the continuance of their professional training, and also insured new classes for admission in September, 1941. In February, 1942 temporary commissions in either the Army or Navy were granted to all physically fit students in all classes of the Medical School and to pre-medical students within 12 months of their admission to the School of Medicine. A continued source of students, deferred by draft boards, but committed to national service on graduation, is thus assured for this and other medical schools of the country.

With the declaration of war on December 8, 1941 the Faculty was at once presented with two problems, the acceleration of the teaching program and the contraction of the teaching staff in order to release physicians for duty with the armed forces. Even before official estimates of their needs were announced by military authorities, it was realized by members of this Faculty that the number of medical personnel to meet both military and civil requirements would likely exceed the number available; and that plans should therefore be contemplated for increasing the size of classes admitted and especially for acceleration of the course of undergraduate training. Consideration of these changes was not advocated—or justified—on educational grounds; they were reluctantly regarded as obligations of medical

schools to make more effective the already enacted deferment of medical students by Selective Service. But the majority of schools were unwilling to urge such action until it was advocated by government officials. The military authorities admitted the increasing need for medical officers but hesitated to advise the universities and medical schools. The Association of American Medical Colleges took the lead and recommended in May, 1941 that "those schools which can do so" increase enrollment by 10 per cent, continue the fourth year classes during the summer and that plans be studied for accelerating the schedule of all classes. Little was done in response to these recommendations; most schools hesitated to act until there could be uniformity. Public opinion had not crystallized, national or governmental direction was not exercised and action was unfortunately delayed.

Hesitation ended with Pearl Harbor. On December 11, the Medical Faculty recommended "that immediate steps be taken to facilitate the graduation of medical students for the duration of the war"; and before January 1, the Medical School announced the decision to conduct courses for all classes throughout the year, beginning with a full Summer Quarter in 1942. Many other schools soon adopted similar plans.

In constructing the schedule for the accelerated program, much thought was given not only to the sequence and arrangement of courses, but also to means for avoiding too great a strain on the health of students and staff—a hazard normally greater than in other fields of education. Several free afternoons weekly during the summer and one full month of vacation were accordingly provided in the new schedule. Each class will be in attendance for 44 weeks in each calendar year. For working out the new time schedules, the School is indebted to the careful studies made by Professor Robert A. Moore.

The new year was scheduled to begin on June 15, for the second, third and fourth year classes, leaving September free for vacation. For the first year class, the vacation was set between commencement and July 13, when the work of the first year began. The next class will graduate in March, 1943, three months ahead of normal schedule. New classes will be admitted and classes will graduate at nine-month intervals. By this plan the full medical course will be completed in three calendar years, the number of graduates thus being increased by about one-third each year.

One of the serious difficulties in the operation of the accelerated program is the inability of many students to meet the costs. About one-fourth of our students depend in part on money earned during one or more summer vacations to pay tuition and living expenses for the following year. The opportunity to earn this support is lost under the new plan. The scholarship and loan funds of the University are quite inadequate to meet the

need. A generous gift for this purpose of \$10,000 from the Kellogg Foundation almost supplies the present requirement, but will soon be exhausted at the present rate of disbursement. There is prospect of Government aid in the form of loans at low interest to meet this problem.

The second problem created by the war—the retention of an adequate staff of instructors—has been even more difficult of solution. General Hospital Unit No. 21 under the direction of Dr. Lee D. Cady and composed of 53 members of the staffs of the Medical School was called to active military duty on January 10, 1942—one of the first University units to be activated. From this General Hospital Unit, another has recently been formed; the 21st Station Hospital Unit with 20 officers, the senior being Dr. Franklin Walton, Assistant Professor of Surgery and Assistant Dean of the School. On January 5, 1942, Medical Specialists Unit No. 72 of the Navy, composed of six officers under the direction of Dr. Frederick Jostes was called to active service. Many other members of the staff have accepted commissions and been ordered to duty in the Army or Navy. Altogether to date 78 members of the staff are absent on leave for military service. The extent of this contribution of medical officers from the School is indicated by the fact that their number is about one-fourth of the total of the active teaching staff. Many more under the age of 45 must doubtless be released, to meet the growing needs for medical officers in the Armed Forces. This will require that many of the older members of the staff be called upon to accept heavy teaching responsibilities at the cost of great reduction in their private practice. Only by transferring more medical service to clinics and hospitals with less in homes and offices can the needs for medical teaching and for medical service to patients be met by the reduced staffs.

A Federal Office of Medical Procurement and Assignment has been established in Washington with local and state committees, for the purpose of meeting military and civilian needs for qualified personnel by the proper distribution of physicians, dentists and veterinarians. The staffs of medical schools are classified periodically and only those are called to military duty who can be released. This wise policy will aid in preserving skeleton staffs of active younger teachers, but can be applied only to a fraction of the number needed by the schools. The most serious problem now confronting the School is to discover and to retain adequate staff replacements. It will be a permanent loss to Medicine unless more effective measures are adopted to retain in academic and scientific works the all-too-rare gifted younger teachers and investigators.

How the strain on students and staff at the higher tempo will be borne, how if at all the educational results will suffer, it is too early to say; but the

signs so far indicate that this Medical School can and will operate on a larger scale, at a faster pace, without change of its primary purpose or lowering of its educational standards. What is almost certain to suffer is fundamental research, the mainspring of important advances of knowledge. But that loss will be more or less offset by the many specific investigations directed toward problems related to the war effort.

The Faculty

At the end of the academic year 1940-41, Dr. Robert J. Terry, Professor of Anatomy since 1899, retired from active duty with the title of Emeritus. No other member of the faculty has given longer or more devoted service to the Medical School, no other has deeper regard and affection of its alumni. His colleagues wish him the fullest satisfaction in well earned leisure, now occupied in continuing his studies in physical anthropology. The School was most fortunate in having on the faculty, Dr. E. V. Cowdry as Professor of Cytology, who accepted the Professorship of Anatomy and Headship of the Department and has carried on the fine traditions of teaching and research established during Dr. Terry's long tenure.

Having reached the age for retirement several other senior members of the Faculty have been appointed to Emeritus Professorships in proud recognition of their distinguished services to the University: Dr. Vilray Blair in Surgery, Dr. Martin F. Engman in Dermatology, Dr. Albert E. Taussig in Medicine and Dr. Willard Bartlett in Surgery. During the War Emergency there will be continued need for the assistance of these experienced teachers in the conduct of their respective departments.

A difficult problem arose in the spring of 1941 from the resignation of two valued heads of important clinical departments. Dr. David Barr, for 17 years Busch Professor of Medicine, resigned to become head of that department at Cornell. Dr. John Whitehorn, Professor of Psychiatry, resigned to succeed Dr. Adolf Meyer at Johns Hopkins. To select and obtain worthy young successors to fill these chairs became even more difficult than first appeared, when the Declaration of War led to urgent and increasing demands for all available young medical specialists for military and other duties outside civil institutions; for all good men who could be spared would feel their first call to be for government duty.

It has become a policy of this school to seek young men for its new heads of departments; it was decided to hold to that policy if possible. Temporary arrangements were therefore necessary for the year 1941-42 in both of these departments. Dr. Harry Alexander generously consented to accept temporary direction of Medicine. Similarly, Dr. David Rioch assumed temporary charge of Psychiatry in addition to his direction of Neurology. Both

have successfully discharged these difficult duties, and have aided in selecting the new heads of these departments.

It is a satisfaction to report that Dr. W. Barry Wood, Jr. has been appointed Busch Professor of Medicine, effective July 1, 1942. He becomes also Physician-in-Chief to the Barnes Hospital, and Director of Medical Services in the Washington University units in the City Hospitals. Dr. Wood is a graduate of Harvard College and before coming to us was Associate in Medicine at Johns Hopkins where he received the M.D. degree in 1936. He is best known for his investigation of experimental pneumonia and its treatment by the sulfonamide drugs. As a member of a Civilian Commission for Infectious Diseases appointed by the Surgeon General, he spent a large part of the past year in a study of pneumonia in one of the Army camps. As a condition of his accepting appointment here, he will continue to serve on this Commission whenever called upon for special duties. By this compromise the Medical School has been able to follow its policy of appointing active young men to its professorships, while allowing them to serve their military assignments.

We are fortunate also in the appointment of Dr. Edwin Gildea, until now Associate Professor of Psychiatry at Yale University, who becomes Professor of Psychiatry here. At Dr. Rioch's request, Dr. Gildea will act also as the administrative head of the department of Neuropsychiatry. Dr. Gildea received the M.D. degree at Harvard in 1924 and has been a member of the department of Psychiatry at Yale for several years. His interest is mainly in the physiological and biochemical basis for type differences in constitution and personality, as related to psychological states. With Dr. Gildea's coming in September, it is expected that the development of psychiatric teaching, begun by Dr. Whitehorn and under difficulties conducted successfully the past year by Dr. Rioch and Dr. Warson, will be expanded for graduate as well as for undergraduate students. The appointment of Dr. Samuel R. Warson as assistant professor of psychiatry began in July, 1941.

With the support and approval of Mr. F. C. Rand, Chairman of the Board of Trustees of the Barnes Hospital and of Bishop John C. Broomfield of the Methodist Episcopal Church, Dr. Frank Bradley, Superintendent of the Barnes Hospital has been appointed Lecturer in Hospital Administration. By this appointment both institutions benefit. Dr. Bradley will inform and guide students of the fourth year class concerning their duties as house officers. His important function as Chairman of the newly established Joint Medical Board and of the Medical Center Administrative Committee has already brought about closer cooperation between the hospitals and in their relations to the Medical School.

For some years it has been felt that the teaching of public health would be strengthened by closer affiliation with the City and County Health Departments. In the spring of 1941, a new Director was selected for the Department of Health of St. Louis County, following the resignation of Dr. T. R. Meyer for military duty. Arrangement was made whereby the new Director, Dr. Edward G. McGavran, was appointed also Associate Professor of Public Health in the School of Medicine. An expanded program of teaching under Dr. McGavran's guidance has been inaugurated. Dr. Bronfenbrenner will retain responsibility for the course.

Promotions to professorial rank during the year include: Dr. Harry L. Alexander as Professor of Clinical Medicine; Dr. French K. Hansel as Associate Professor of Clinical Otolaryngology; Dr. Carl R. Wegner as Assistant Professor of Clinical Obstetrics and Gynecology; and Dr. Daniel W. Myers as Assistant Professor of Clinical Medicine.

With the loss of staff members from every department for military duty and because of the growing difficulties of securing replacements or of training new personnel, it becomes necessary to utilize much more fully than heretofore all members of the Medical School for duties for which each is best qualified, without regard to his normal departmental appointment. This emergency policy will mean heavier duties and some interruption of research programs, but will also have some important advantages. A regrouping of staffs, by bridging departmental boundaries, will bring a closer integration of instruction that is likely to be of great benefit to medical education.

An illustration of this plan is the closer affiliation now arranged between the departments of Pharmacology and Biological Chemistry. Under the leadership of Professor C. F. Cori a group of exceptionally able and active bio-chemists have made notable progress in investigating the enzymic reactions concerned with carbohydrate metabolism. The individuals happen to hold academic appointment in the department of Pharmacology, yet are especially qualified to take part in the teaching of bio-chemistry. The department is greatly strengthened by making them also members of the staff of Biological Chemistry.

The title of Dr. C. F. Cori, heretofore Professor of Pharmacology has been changed to Professor of Pharmacology and Biological Chemistry. Dr. Arda Green has been appointed Assistant Professor of Biological Chemistry, retaining also appointment as Research Associate in Pharmacology. Dr. Gerti Cori, formerly Research Associate in Pharmacology, becomes Research Associate in Pharmacology and Biological Chemistry. Dr. Herman Kalckar, Research Associate in Radiology, is appointed also Instructor in Biological Chemistry. Dr. Sidney Colowick is appointed Instructor in Biological

Chemistry and Pharmacology (at present engaged full time on O. S. R. D. research under Dr. Cori's direction). Each of these members of the staff will participate in both undergraduate and graduate instruction in both departments; otherwise their departmental duties and responsibilities are unchanged. Dr. Cori remains the administrative head of the department of Pharmacology, while Dr. Shaffer remains Professor of Biological Chemistry and titular head of that department.

Similar arrangements are contemplated in other departments, with the object not only of meeting the present urgent need for more economical use of the reduced staffs, but also for the benefit that will come from closer contact between departments and the integration of instruction.

The routine activities of the Dean's Office have been materially increased because of the war. To fill the place of Dr. Franklin E. Walton, Assistant Dean, who was called to active duty with General Hospital No. 21, two administrative appointments have been made: Dr. Carlyle Jacobsen as Assistant Dean; and Dr. Leo Wade as Faculty Adviser on Internships.

It is with both regret and satisfaction that I record the resignations of three members of the faculty to accept positions in other institutions: Dr. Gordon H. Scott, Associate Professor of Histology to become Professor of Anatomy at the University of Southern California; Dr. Louis A. Julianelle, Associate Professor of Applied Bacteriology and Immunology in Ophthalmology to become Director of the Public Health Research Institute of the City of New York; and Dr. Thomas P. Findley, Jr., Assistant Professor of Clinical Medicine to become an Assistant Professor of Medicine at Tulane University.

The faculty and students have been fortunate in having an opportunity to study under and attend special lectures by members of the faculty of other universities. Visiting Professors were Dr. A. J. Carlson, Visiting Professor of Physiology (from the University of Chicago), Dr. J. B. Baumberger, Visiting Professor of Cytology (from Stanford University) and Dr. W. C. Ma, Visiting Associate Professor of Anatomy (from the Peking Union Medical College). Special lectures have been given by Dr. Edgar Allen, Professor of Anatomy, Yale University; Dr. William Boyd, Professor of Pathology, University of Toronto; Dr. Carl Hartman, Professor of Zoology, University of Illinois; Dr. Paul Hanzlik, Professor of Pharmacology, Stanford University; Dr. Eugene Kellersberger, General Secretary for the American Mission to Lepers in Central Africa; Dr. Eugene Landis, Professor of Medicine, University of Virginia; Dr. John Musser, Professor of Medicine, Tulane University (Leo Loeb Lecture); Dr. A. Purdy Stout, Associate Professor of Surgery, Columbia University (Alpha Omega Alpha Lecture);

and Dr. George B. Wislocki (A.B., Washington University, 1912), Parkman Professor of Anatomy, Harvard University (Robert J. Terry Lecture).

There were during the year three deaths among the faculty. Dr. Max A. Jacobs, Assistant Professor of Clinical Otolaryngology on January 9, 1942; Dr. Warren R. Rainey, Assistant Professor of Clinical Surgery on July 28, 1941; and Dr. Hans L. Kleine, Assistant in Clinical Obstetrics and Gynecology on September 21, 1941 while on active duty with the U. S. Army.

Gifts and Grants

Early in December of 1941 one of the largest single gifts in recent years to the School of Medicine was made by Mr. and Mrs. Wallace Renard of St. Louis. Mr. and Mrs. Renard have for many years been interested in the development of Washington University. After thorough study and consultation with members of the Administration and Faculty they determined on a gift of \$250,000, the income from which is to be used for support of the Department of Neuropsychiatry. This department was made possible by a grant from the Rockefeller Foundation four years ago and it is most gratifying to see a beginning toward a permanent endowment for this most important activity of the University.

The most generous gift of the Kellogg Foundation of \$10,000 as a fund for loans and scholarships under the accelerated programs has already been referred to. It is anticipated that additional funds, either from private or governmental sources, will be required to continue the year-round attendance of medical students in the University.

The minutes of the Executive Faculty for the year record gifts and grants from Commodore Louis D. Beaumont, Burdick Corporation, Jane Coffin Childs Memorial Fund, Ciba Pharmaceutical Products Company, Commonwealth Fund, Corn Industrial Research Foundation, Delta Gamma Fraternity, Dr. Clarence J. Gamble, International Cancer Research Foundation, Dr. Kiyoshi Inouye, Eli Lilly Company, Josiah Macy, Jr. Foundation, Mr. Edward Mallinckrodt, Mr. Morton J. May, John and Mary R. Markle Foundation, Mead, Johnson and Company, National Defense Research Council, National Foundation for Infantile Paralysis, National Research Council, Mr. Edgar Queeny, Rockefeller Foundation, Scottish Rite Fund, Schieffelin and Company, Mr. Julius Simon, Colonel Fred A. Wilson, Winthrop Chemical Company, Mr. David P. Wohl, and Dr. and Mrs. F. E. Woodruff.

In most instances these gifts and grants have been made in support of specific research projects, many of which have a definite relation to the war effort. It is not possible to mention each of these investigations but the broad fields of study are worthy of note; enzyme chemistry, physiology of the nervous system, gerontology, hematology, endocrinology, anaphylaxis,

viral diseases, metabolism of proteins, cancer, chemotherapy, renal function, the prevention of shock, and the mechanism and conservation of vision. Although there will probably be considerable reduction in certain types of research during the years of the war, it is to be hoped that the efforts of the faculty will continue to enjoy the confidence of those who wish to support the advancement of scientific knowledge.

It is appropriate here to mention the activities and prospects of the Oscar Johnson Institute and the McMillan Hospital. Erected in the same building to provide excellent facilities for hospital and research laboratories for diseases of eye, ear, nose and throat, circumstances have so far restricted the full use of these facilities.

Of the McMillan Hospital only the out-patient department has been operated; funds for completing and conducting the hospital have been lacking. Arising from the present great shortage of hospital accommodations in St. Louis, there is now some hope of securing a grant that will permit equipment of this hospital. About 150 additional hospital beds, now urgently needed, may thus be added in the Medical Center.

Conduct of the research laboratories of the Oscar Johnson Institute has been made possible on a moderate scale by funds supporting the teaching departments of Ophthalmology and Oto-laryngology. For a time these funds were much augmented by term grants from the Commonwealth Fund and other foundations for special research projects. These special term grants are no longer available and the researches underway in these departments must be curtailed. For some years the free space has been utilized for research supported by several other departments. Research Pathology under Dr. Leo Loeb, Neuropsychology and Bio-physics under Dr. George Bishop, the laboratories of Internal Medicine and more recently of Neuropsychiatry have been quartered in this fine institute building. But all are hampered by inadequate support. The laboratory needs for its full effectiveness as an Institute for Medical Research, a substantial endowment fund. Already many noteworthy contributions have come from the association in this building of several staffs, the members of which have worked in close cooperation. The product would be far greater with adequate support to hold a representative staff of investigators, commensurate with the facilities of this Institute.

Two Professors Emeriti, Dr. Leo Loeb and Dr. Robert J. Terry, continue their research activities despite retirement from administrative duties. The preeminent position of these two in their respective fields of pathology and anatomy continue to represent one of the University's important contributions to medical and graduate education.

Educational Program

The enrollment in the undergraduate course as candidates for the degree of Doctor of Medicine has for some years reached the limit considered optimum for existing facilities and staff. During the year 1941-42 the enrollment was increased somewhat in the third year and totaled 359, distributed as follows:

First Year, 81; Second Year, 83; Third Year, 102; Fourth Year, 93.

The number of applicants, including those from other medical schools seeking admission to the upper classes, totaled more than 800. Students enrolled in the School come from 39 states and six foreign countries.

In September, 1941, two British medical students, Mr. Cadman from the University of Liverpool and Mr. O'Hea from Glasgow University, transferred to Washington University under scholarship from the Rockefeller Foundation. Within a few weeks these men joined the scheme of American medical education without sacrifice of their own personality and training. They will graduate in December, 1942 and return to Britain. The good wishes of the entire faculty and student body will go with them.

One hundred and fourteen applicants were accepted to enter the School in September, 1941. Ninety-three members of the fourth year class received the degree of Doctor of Medicine in June, 1942. These graduates were appointed to internships in 33 hospitals rather widely distributed in different sections of the country. Fifty of the ninety-three are in St. Louis hospitals.

The number of applicants for the 1942-43 session was about 950. Of these 121 were accepted. The present enrollment (for 1942-43) is 373, the largest in the history of the School.

Aside from the alterations necessitated by the accelerated program, only a few changes have been effected in the curriculum. These may be discussed in two groups; introduction of new courses and reorientation of present courses in relation to adequate preparation of students for military service; and the establishment of conjoint courses in clinical subjects.

With the organization of the Office of Civilian Defense it became evident that all medical students should receive instruction in the basic principles of first-aid. Accordingly, a graded course of 12 hours was organized by Lieutenant Colonel Perry for each of the four classes and given during the months of January and February of 1942. Provision has also been made for a similar course as a part of the regular work of the first year for all entering classes. In line with a recommendation of the Association of American Medical Colleges, a committee has been appointed to survey the present teaching activities in relation to military needs and to recom-

mend additional lectures or increased emphasis to insure satisfactory preparation of the student for service in the Armed Forces.

The dispersal of American troops to all parts of the world, especially to the tropics and to the Orient, is responsible for other changes in the curriculum. In the four corners of the earth, diseases and conditions not seen in the Continental United States are encountered. The doctor must therefore receive some training in the diagnosis and treatment of tropical diseases. A corollary of this is greater emphasis on preventive medicine. In the accelerated program an additional eleven hours has been allotted to the Department of Public Health and provision has been made for a twenty-two hour course in parasitology. Further orientation in this direction may become desirable as the specific medical problems of global warfare are more definitely crystallized.

The conservation of time and effort in the accelerated schedule is of the greatest importance. In order to avoid unnecessary duplication and to integrate the subject matter more effectively two conjoint courses have been inaugurated, one, an introduction to clinical medicine and the other, syphilology. Committees under the chairmanship of Dr. Carl Moore and Dr. Malcolm Cook respectively have arranged for integrated lectures, demonstrations, clinics and clerkships on these subjects. Adequate instruction in syphilology is of special significance in connection with the venereal disease campaign of the United States Public Health Service. Experience with this beginning will serve as a guide for future development in the field of interdepartmental teaching.

Alumni

The Washington University Medical Alumni Association under the presidency of Dr. Charles A. Stone, '08, has continued to render valuable service to the School. In April the second Robert J. Terry Lecture, sponsored by the Association was presented in the amphitheatre of the School by Dr. George B. Wislocki, Parkman Professor of Anatomy at Harvard University. On the Saturday before graduation the Association was host to the Faculty and Senior Class at a dinner at the DeSoto Hotel. Functions of this sort serve to bring the faculty in closer contact with the alumni and should become an annual activity. The Association renewed in 1941-42 the scholarship given for some years to a deserving student, known as the Alumni Scholarship.

The Editorial Board of the Washington University Medical Alumni Quarterly was reorganized last January under the direction of Professor Robert A. Moore as Editor. At the request of the officers of the Alumni Association, Dr. Moore generously consented to assume this important assignment, made vacant by the withdrawal for military duty of the former

Editor, Dr. H. L. White. On the new Editorial Board three members have been chosen by the Alumni Association: Dr. Louis H. Jorstad, '24, Dr. James W. Bagby, '33, and Dr. Leo J. Wade, '38. The members chosen by the University are, Dr. R. J. Terry, '95, Dr. Alexis Hartmann, '21 and Dr. Robert Elliott, '36. With rotating terms and an editorial staff appointed by the Board, the continued existence and development of the Medical Alumni Quarterly is assured under joint sponsorship of the Alumni and of the University.

Respectfully submitted,

Philip A. Shaffer, Dean.

The Use of the Egg Protection Test for the Recognition of St. Louis Encephalitis in Man. R. J. Blattner and J. V. Cooke: *J. Infect. Dis.*, 70: 226-230, 1942.

The presence of St. Louis encephalitis protective antibodies as demonstrated by an egg protection test, utilizing the in vitro serum-virus and passive protection technics; vital staining with trypan blue was found to be of considerable help in interpreting results.

In three instances specific St. Louis encephalitis antibodies were recognized after clinical illnesses diagnosed as encephalitis.

The authors feel that the egg protection test is a simple, economical and objective method for the detection of virus immune bodies and that it is of value not only in the diagnosis of individual cases of encephalitis, but that it may be of value in epidemiological studies where the disease is prevalent.

Studies on the Early Recognition of Myocardial Disease by Use of the Vibrocardiogram. William B. Kountz and John R. Smith: *South. M. J.*, 35: 713-720, 1942.

The authors discuss the changes in the curves of total cardiac vibrations recorded by means of the cathode ray vibrocardiograph. Their subjects were divided into three groups, normal, patients with heart disease and patients suspected of having heart disease. Two curves were taken on each subject, one at basal condition and another after activity. Evidence is presented which suggests that in myocardial disease or weakness, changes in total cardiac vibration may occur before other signs of weakness of the heart muscle develop.

Publications by the Staff of the School of Medicine

WASHINGTON UNIVERSITY

June-September, 1942

- Bartley, S. Howard. Visual sensation and its dependence on the neurophysiology of the optic pathway. *Biol. Symposia*, v. 7: 87-106, 1942.
- Bishop, George H., and O'Leary, James L. The polarity of potentials recorded from the superior colliculus. *J. Cell. & Comp. Physiol.*, v. 19: 289-300, June 1942.
- Bishop, George H., and O'Leary, James L. Factors determining the form of the potential record in the vicinity of the synapses of the dorsal nucleus of the lateral geniculate body. *J. Cell. & Comp. Physiol.*, v. 19: 315-331, June 1942.
- Brown, James Barrett. Treatment of war injuries to the face. *Bull. Am. Coll. Surgeons*, v. 27: 132-135, April 1942.
- Brown, James Barrett, and McDowell, Frank. Epithelial healing and the transplantation of skin. *Ann. Surg.*, v. 115: 1166-1181, June 1942.
- Brown, James Barrett, and McDowell, Frank. Review of reconstructive surgery of the face, 1940-1942. *Laryngoscope*, v. 52: 489-504, June 1942.
- Byars, Louis T. Free full thickness skin grafts. Principles involved and technique of application. *Surg., Gynec. & Obst.*, v. 75: 8-20, July 1942.
- Colowick, S. P., and Sutherland, Earl W. Polysaccharide synthesis from glucose by means of purified enzymes. *J. Biol. Chem.*, v. 144: 423-437, July 1942.
- Cooke, Jean V. The incidence of acute leukemia in children. *J. A. M. A.*, v. 119: 547-550, June 13, 1942.
- Cooke, Jean V., and Blattner, Russell J. The use of the egg protection test for the recognition of St. Louis encephalitis in man. *J. Infect. Dis.*, v. 70: 226-230, May-June 1942.
- Cramer, W., and Stowell, R. E. XCVIII. Osteosis cutis in methylcholanthrene epidermal carcinogenesis in mice. *Arch. Dermat. & Syph.*, v. 46: 276-282, Aug. 1942.
- Crossen, H. S. The menace of "silent" ovarian carcinoma. *J. A. M. A.*, v. 19: 1485-1489, Aug. 29, 1942.
- Edwards, Joseph C., Findley, Thomas, and Clinton, Etta. The effect of sympathectomy on renal blood flow in essential hypertension. *Surgery*, v. 12: 64-67, July 1942.
- Elman, Robert, and Eckert, C. L. Treatment of acute perforative peritonitis. The importance of operation, oxygen inhalations, plasma transfusions and the sulfonamides. *J. Missouri M. A.*, v. 39: 193-198, July 1942.
- Elman, Robert, Sachar, Leo A., Horwitz, Abraham, and Wolf, Harriet. The experimental production of hypoalbuminemia by fasting. *J. Lab. & Clin. Med.*, v. 27: 1183, June 1942.
- Elman, Robert, Sachar, Leo A., Horwitz, Abraham, and Wolf, Harriet. Regeneration of serum albumen with hydrolyzed protein in chronic hypoproteinemia produced by diet. An experimental study. *Arch. Surg.*, v. 44: 1064-1070, June 1942.
- Elman, Robert, Weiner, D. O., and Bradley, R. N. Intravenous injections of amino-acids (hydrolyzed casein) in postoperative patients. *Ann. Surg.*, v. 115: 1160-1165, June 1942.
- Elman, Robert, and White, Abraham. Preparation of tryptophane-containing acid hydrolysates of proteins suitable for intravenous administration. *J. Biol. Chem.*, v. 143: 797-798, May 1942. (Letter to the editors.)

- Eyermann, Charles H. Food allergy. *J. Am. Dietet. A.*, v. 18: 370-374, June 1942.
- Gardner, Ernest D. Nerve terminals associated with the knee joint of the mouse. *Anat. Rec.*, v. 83: 401-419, July 1942.
- Garol, Hugh W., von Bonin, Gerhardt, and McCulloch, Warren S. The functional organization of the occipital lobe. *Biol. Symposia*, v. 7: 165-192, 1942.
- Graham, E. A., and Mueller, C. B. Influence of hypophysectomy on epithelization of wounds and on fibroplasia. *Proc. Soc. Exper. Biol. & Med.*, v. 50: 139-141, May 1942.
- Hartmann, Alexis F., Barnett, Henry L., Powers, John R., and Benward, John H. Salicylate intoxication in infants and children. *J. Pediat.*, v. 21: 214-223, Aug. 1942.
- Heinbecker, Peter, White, H. L., and Rolf, Doris. Effects of the removal of the anterior lobe of the hypophysis on some renal functions. *Am. J. Physiol.*, v. 136: 584-591, June 1942.
- Heinbecker, Peter, White, H. L., and Rolf, Doris. Relation of the adeno and the neurohypophysis to insulin sensitivity and sugar tolerance in the dog. *Am. J. Physiol.*, v. 136: 592-594, June 1942.
- Hobbs, John E. Primary carcinoma of the fallopian tube: case report. *South. M. J.*, v. 35: 733-737, Aug. 1942.
- Hunter, F. Edmund. Occurrence of sphingomyelin in tissues of the cat. *J. Biol. Chem.*, v. 144: 439-445, July 1942.
- James, William M. The surgical removal of corneal scars. *Am. J. Ophth.*, v. 25: 672-684, June 1942.
- Keyes, E. Lawrence. Further experience with the exclusion operation for the treatment of fistula of the small intestine. *South. M. J.*, v. 35: 823-837, Sept. 1942.
- Kountz, William B., and Smith, John R. Studies on the early recognition of myocardial disease by use of the vibrocardiogram. *South. M. J.*, v. 35: 713-720, Aug. 1942.
- Lansing, Albert I. Increase of cortical calcium with age in the cells of *Elodea canadensis*. *Biol. Bull.*, v. 82: 385-391, June 1942.
- Lansing, Albert I. Increase of cortical calcium with age in the cells of a rotifer, *Euchlanis dilatata*, a planarian, *phagocata* sp., and a toad, *Bufo fowleri*, as shown by the microincineration technique. *Biol. Bull.*, 82: 392-400, June 1942.
- Loeb, Leo, and Blumenthal, H. T. Effects of Progesterone on the sex organs and on the production of placentoma in the female guinea pig. *Arch. Path.*, v. 34: 49-66, July 1942.
- Loeb, Leo, and Blumenthal, H. T. Two antagonistic effects of under-feeding on the adrenal cortex of the guinea pig. *Am. J. Path.*, v. 18: 615-631, July 1942.
- Loeb, Leo, Suntzeff, V., Blumenthal, H. T., and Kirtz, M. Moskop. Effect of weight on the development of mammary carcinoma in various strains of mice. *Arch. Path.*, v. 33: 845-865, June 1942.
- Miller, Mary Lucy. The neutral steroids in the urine of individuals with benign hypertrophy of the prostate. *J. Urol.*, v. 47: 846-851, June 1942.
- Moore, Robert A., Bittinger, Isabel, Miller, Mary L., and Hellman, Louis M. Abortion in rabbits fed a vitamin K deficient diet. *Am. J. Obst. & Gynec.*, v. 43: 1007-1012, June 1942.
- Moore, Robert A., Spies, Tom D., and Cooper, Zola, K. XCIX. Histopathology of the skin in pellagra. *Arch. Dermat. & Syph.*, v. 46: 100-111, July 1942.
- Post, Lawrence T. Aniseikonia. *South. M. J.*, v. 35: 649-652, July 1942.
- Post, Lawrence T. Lifelong care of the eyes: Chairman's address. *J. A. M. A.*, v. 119: 921-923, July 18, 1942.

- Probststein, J. G., and Londe, Sol. Hepatic function and the formation of hippuric acid: response to the administration of aminoacetic acid and sodium benzoate in patients with subnormal capacity for synthesis. *Arch. Surg.*, v. 45: 253-260, Aug. 1942.
- Russell, William O. Plastic cover slips. A critical evaluation. *J. Tech. Methods*, 22: 65-70, July 1942.
- Russell, William O., and Stahl, William C. Fatal poisoning from potassium thiocyanate treatment of hypertension. (Report of a case and review of the literature.) *J. A. M. A.*, v. 119: 1177-1181, Aug. 8, 1942.
- Scott, Gordon H., and Packer, D. M. A cryostat of new design for low temperature tissue dehydration. *J. Tech. Methods*, 22: 85-96, July 1942.
- Scott, Wendell G., and Lionberger, John R. Studies of the pulmonary vessels by means of body-section radiography. *Radiology*, v. 39: 157-166, Aug. 1942.
- Senturia, Ben. H., and Sulkin, S. Edward. The etiology of myringitis bullosa hemorrhagica. Preliminary report. *Ann. Otol., Rhin. & Laryng.*, v. 51: 476-482, June 1942.
- Stowell, R. E. Tertiary butyl alcohol as a microtechnical reagent. *J. Tech. Methods*, 22: 71-74, July 1942.
- Wade, Leo J. The effect of pregnancy upon experimental tuberculosis in rabbits. *Am. Rev. Tuberc.*, v. 46: 93-100, July 1942.
- White, H. L., Findley, Thomas, Edwards, J. C. and Clinton, Etta. Intravenous urography: a test of renal function. *J. Urol.*, v. 48: 119-125, July 1942.
- Womack, Nathan A., and Hempelmann, Louis H. The pathogenesis of mixed tumors of the salivary gland type. *Ann. Surg.*, v. 116: 34-42, July 1942.
- Wood, W. Barry, Jr., and Aranow, Henry. Staphylococcal infection simulating scarlet fever. *J. A. M. A.*, v. 119: 1491-1495, Aug. 29, 1942.
- Wu, Y. K., and Loucks, H. H. Resection of the esophagus for carcinoma. An analysis of experiences in eleven cases. *J. Thoracic Surg.*, v. 11: 516-528, June 1942.

The Menace of "Silent" Ovarian Carcinoma. H. S. Crossen: *J. A. M. A.*, 119: 1485-1489, 1942.

The symptomless onset and progression to incurability of ovarian carcinoma is stressed. Measures for earlier detection of the disease are advised. These consist of; removal of involuting ovaries whenever the abdomen is opened under circumstances which permit such removal, regular periodic pelvic examination at six month intervals, and utilization of every opportunity afforded by anesthesia for minor vaginal operation to make accurate palpation of the ovarian region.

***Buy War Stamps and Bonds
Then Contribute to Alumni Fund***

News from the Medical School and Affiliated Hospitals

The Chancellor announced the following gifts to the Medical School between July 1 and September 30, 1942: From The Commonwealth Fund, an appropriation of \$9,800 to Dr. Robert Moore in the Department of Pathology for functional studies of autopsy material; From The Commonwealth Fund, an appropriation of \$7,800 to the Institute of Radiology for two years' study of radioactive phosphorus in the treatment of cancer by Dr. Louis H. Hempelmann, Jr.; From The John and Mary R. Markle Foundation, an appropriation of \$2,070 annually for two years to the Department of Pathology in support of Dr. William Russell's study of the behavior and growth of tumors of the nervous system; From Mead Johnson and Company, an appropriation of \$2,760 as a grant-in-aid in support of studies in the Department of Surgery under Dr. Robert Elman; From The Rockefeller Foundation, an appropriation of \$13,920 for expenses of increased use of the cyclotron during the year 1942-43; From the Winthrop Chemical Company, a fellowship of \$1,200 in continued support of investigations on the synthetic estrogenic compounds under the direction of Dr. MacBryde in the Department of Medicine; From the Julius Rosenwald Fund, \$1,500 in continued support of work established at Homer Phillips Hospital by the Department of Neuropsychiatry; From The Rockefeller Foundation, \$1,909.84 for the tuition and living expenses of two British medical students, Mr. Cadman and Mr. O'Hea; From Mr. Edward Malinckrodt, Jr., \$1,800 in continued support of a fellowship in Pediatrics; From the Alumni Association of the School of Medicine, \$30 for the Alumni Association Fund; From the Burdick Corporation, \$1,440 for the year 1942-43 for research under the direction of Dr. William Kountz; and From The Rockefeller Foundation, \$1,200 plus tuition and fees for a British medical student, Samuel Oleesky, for one year beginning July 24, 1942.

The need for rotating internships has become more acute because of the present emergency in which we are engaged. For this reason and because of other advantages nine appointments for one year have been made, effective April, 1943. This will permit a service of four months in St. Louis Maternity, St. Louis Children's and Barnes Hospitals, respectively. It has been proposed that because of the seasonal variation of work in pediatrics and obstetrics that it would probably be desirable not to have the entire four months in one block on any service. Periods of two months and

the two periods later of one month each would afford a more valuable service to the interne. After the war when a longer period of internship will be possible, the duration of the rotating internship may be lengthened with even the possibility of including additional services. A second type of rotating internship has been made possible by St. Louis Maternity Hospital and the Missouri Pacific Hospital. There will be an affiliation of services in obstetrics, medicine and surgery. Dr. Willard Allen, Chief of Staff of St. Louis Maternity Hospital and Mr. Harry J. Mohler, President of the Missouri Pacific Hospital Association have an arrangement which is mutually beneficial at the present time when war conditions make it virtually impossible to fill single service internships. There will be six internship appointments, four of the interns will serve at one time at Missouri Pacific Hospital while two are on the obstetrical service at the Maternity Hospital. The time allotted to individual services is planned so that there are four months of obstetrics, medicine and surgery, respectively. This means that eight months will be spent at the Missouri Pacific Hospital. The majority of staff men at the Missouri Pacific Hospital are on the faculty of Washington University. Dr. A. O. Fischer and Dr. Ernest Sachs are among those on the surgical staff.

A portrait of Dr. Nathaniel Allison, Dean of the Medical School, 1920-1923, was given to the School by his sister, Mrs. Frances Allison Krebs, and is hanging in the Library.

Recently another type of non-professional worker has been added to the nursing service in the Barnes Hospital ward unit. She is the ward secretary. She has taken on many of those clerical duties which break into the professional activities of the head nurse and general staff group and have consumed too much of their time. From the experience the hospital has had, she is fast becoming an indispensable part of the hospital personnel.

Generally speaking, she should have been graduated from high school, and, since her duties are largely clerical, a knowledge of typing is desirable. It is important that she be alert and that she have a good approach to people as one of her assignments may be meeting and directing visitors. She should be located centrally in the unit, either at the head nurse's station or at some other convenient place.

Among the duties found to be delegated to the ward clerk are listing names on weekly time sheets, making midnight census reports and other hospital ward reports, preparing requisitions and labels for file cabinets, drawers, etc. She may also be given such responsibilities as transferring the records of temperature, pulse and respiration, and weight on the graphic

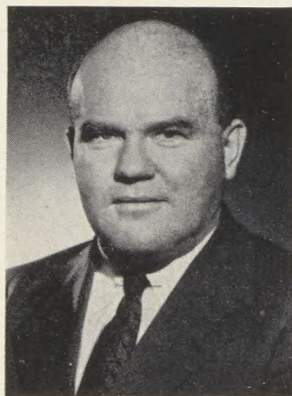
charts; completing and disposing of records of discharged patients; and distributing and collecting charts for doctors' rounds. Answering the telephone and delivering the messages to the proper persons; making telephone calls, both routine and as instructed; and directing visitors, and seeing that they leave promptly at the end of the visiting hour are also included among the numerous activities which are being assigned to the ward clerk thus releasing the busy head nurse for the more important administrative and supervisory responsibilities on the ward.

She must be a rather unusual type, being able to assume responsibility, and yet at the same time, recognize the nurse as her superior. The relationship is similar to that of an administrator and his secretary.

New appointments to the School of Medicine include: Dr. Carlyle F. Jacobsen, as Assistant Dean, retaining his appointment as Professor of Medical Psychology; Dr. Arda Green, as Assistant Professor of Biological Chemistry, retaining her position as Research Associate in Pharmacology; Dr. Edgar S. Hill, as Instructor in Biological Chemistry. (Dr. Hill is also Assistant Professor in the School of Dentistry); Dr. A. Clyde Brooks, as Assistant in Clinical Medicine; Dr. Margaret Gildea, as Instructor in Psychiatry; Dr. Ray D. Williams, as Instructor in Clinical Medicine; Dr. Charlotte McLeod, as Research Fellow in Medicine; Mrs. Frances K. Graham, as Assistant in Medical Psychology; and Dr. John A. Saxton, as Assistant Professor of Pathology.

Dr. Edwin Gildea has assumed his duties as Professor of Psychiatry. At Dr. Rioch's request, Dr. Gildea will also serve as Administrative Head of the Department of Neuropsychiatry. Dr. Rioch will, however, remain a member of the Executive Faculty.

A grant of \$241,000 federal funds needed to provide 160 new hospital beds on five unused floors of McMillan Hospital, 517 South Euclid Avenue, has been made to the trustees of Washington University. McMillan Hospital, adjacent to Barnes Hospital, occupies the first eight floors of the 14-story building which also houses the Oscar Johnson Institute for research in eye, ear, nose and throat diseases. It was erected 11 years ago. The recent survey of hospital facilities in St. Louis by the St. Louis Social Planning Council revealed approxi-



Dr. Edwin Gildea

mately 775 more hospital beds are needed to serve this area adequately. Barnes Hospital has to turn patients away almost daily, and the additional space will take the strain off present facilities. The grant was made under the Lanham act which was passed to provide increased hospital space in congested war production areas.

Dr. Mildred Trotter, Associate Professor of Anatomy, has been appointed Associate Editor of the American Journal of Physical Anthropology.

The Department of Medicine has made quite a few changes in the last four months.

The changes in physical plant consist of; opening and remodeling the old operating rooms in Barnes and opening the tenth floor of Oscar Johnson Institute. One of the old operating rooms is being transformed into a library for the medical house staff. This will have the current journals, the late monographs and the standard works of medicine. Another will be made into a class room. The old surgical amphitheatre will be repainted and staff rounds will be held there. Dr. Wood and Dr. Alexander will have offices on the third floor. The tenth floor of Oscar Johnson Institute will be divided into research laboratories in allergy, cardiology and infectious diseases. The Department of Hematology will remain on the second floor of the clinic building but they have expanded to occupy quarters formerly used by bacteriology. There has been an addition of a side room to each ward for care of critically ill patients.

The changes in the schedule are as follows: There will be ward rounds on Monday, Wednesday and Friday for the house staff and seniors. One day each week Dr. Wood will make rounds on male and female wards. The other two days will be taken care of by the attending man. There will be rounds in neurology and psychiatry on Tuesday and Thursday. Rounds on metabolism ward will be held as usual on Saturday morning. There is a history meeting on Wednesday from 12 to 1 where all patients discharged during the previous week on the ward service are discussed. Grand rounds will be held from 9:30 to 10:30 on Thursday so all doctors can attend and still attend dispensary. Staff Journal Club, an addition to the schedule, will be held from 12:00 to 1:00 on Friday. The C. P. C. in conjunction with the Department of Pathology is conducted as usual except the whole third and fourth year class attend and the proceedings are published in the Journal of the Missouri Medical Association. There is another conference for the house staff held by Dr. Wood and Dr. R. A. Moore in which all cases from the medical service are presented and the pertinent gross and microscopic findings are shown.

Two new services have been added to the first year of internship. They are the Laboratory Service and the Accident Room at City Hospital. The internship is now planned on a nine month basis and the last three months will be as assistant resident.

The third year schedule has been changed. All teaching will be done at City Hospital No. 1. Dr. B. Taussig will be chief of service. Dr. Wood and Dr. Goldman will make rounds once a week. Dr. Carl Harford will be in charge of Isolation Service. The junior course there will be entitled War Medicine and include study of contagious diseases common in an army camp. Dr. Harford and Dr. Hageman will teach this class.

The second year class is called conjoint medicine. It is a course in physical diagnosis in cooperation with departments of surgery, obstetrics, otolaryngology, pediatrics, and ophthalmology. There are also a series of lectures on the physiological interpretation of signs and symptoms of various disease processes.

The medical specialty clinics have been abolished for the duration and there are Medical Clinic No. 1 and No. 2 in the charge of Dr. A. Goldman and Dr. A. Strauss.

Changes in personnel consist of the abolition of the 18 month internship. The wards now are handled by an assistant resident and two internes. The private service will be staffed mainly by interns who enter for that service.

Since the publication of the April issue of the bulletin there have been a few changes in the Barnes Hospital House Staff. Through error in the April issue the following interns in the Department of Medicine were omitted: Dr. Henry Graham, Cornell, '41; Dr. Robert Koch, Washington University, '40; Dr. Leon Kahn, Washington University, '41; Dr. Frank Stevens, Vanderbilt University, '41; Dr. Roy Ahrens, Washington University, '41; and Dr. S. P. Martin, Washington University, '41. Dr. H. S. J. Walker, Washington University, '41; Dr. Henry Graham, Cornell University, '41; Dr. Leon Kahn, Washington University, '41; and Dr. Norman Gale, Kansas University, '40; entered the Army. Dr. Lee E. Ellman, Washington University, '42, intern in dentistry, entered the Navy and his work is taken over by Dr. R. Jerry Bond, Washington, '41. Dr. Cyril J. Costello, University of Texas, '39, intern in surgery is on leave of absence due to illness.

At the St. Louis Children's Hospital, Dr. Sam Gollub, Washington University, '41; and Dr. Charles Freeman, University of Oklahoma, '41, entered the Army and Dr. Mary McFayden Bishop, Washington University, '40, has been given leave of absence on account of illness.

In Ophthalmology, Dr. W. H. Diehl, Jefferson Medical College, '27, has entered the Army. Dr. E. N. Robertson, Washington University, '37, and Dr. V. A. Toland, Creighton University, '36, have been appointed Resident and Assistant Resident respectively. Dr. R. Scobee, University of Texas, '39, is Assistant in Ophthalmology at Washington University.

At the St. Louis Maternity Hospital, Dr. E. H. Keys, Jr., Washington University, '39; and Dr. R. Wolf, University of Rochester, '39, have entered the Army. The following house officers were unable to accept appointment: Dr. Margaret Carter, Washington University, '36; Dr. C. R. Sias, University of Rochester, '38; Dr. S. E. Ross, Washington University, '41; and Dr. W. L. Topp, Washington University, '41.

In Pathology, Dr. Charles Williams, Washington University '41, reported for duty with the General Hospital of Albany Medical College on July 15.

With deep regret, the death of Dr. Hugo Ehrenfest, Professor Emeritus of Obstetrics and Gynecology and Associate Obstetrician and Gynecologist to the St. Louis Maternity Hospital, is recorded.

Changes in the School of Nursing include the appointments of Miss Mildred Seyler, Instructor in Surgical Nursing; Miss Florence Beltt, Assistant Nursing Arts Instructor; and Miss Irma Kokes, Assistant Science Instructor; and the resignations of Miss Pauline Wylie, Mrs. Josephine Oakes, and Miss Lillian Fisher.

The following have been given leave of absence for duty with the Armed Forces: Lt. Col. J. B. Brown, Major Robert Bartlett, Major Justin Cordonnier, Major Sol Londe, Major Howard Rusk, Major Robert Votaw, Lt. James W. Bagby, Lt. Robert Elliott, Lt. Henry Graham, and Lt. Leon Kahn.

Appointments to the staffs of the hospitals include: Dr. A. Clyde Brooks, Assistant Physician to the Barnes Hospital; Dr. Ray Williams, Assistant Physician to the Barnes Hospital; Dr. Harold Scheff, Assistant Physician to the Barnes Hospital; Dr. G. O'Neil Proud, Resident in Otolaryngology at the Barnes, McMillan and St. Louis Children's Hospital; Dr. David Rothman, Assistant Gynecologist to the Barnes Hospital; and Dr. George Manning, Assistant Physician to the Washington University Clinics.

At the time of his departure from St. Louis, Dr. Thomas Wesson resigned from the staff of the Barnes and St. Louis Children's Hospital and the Washington University Clinics.

Construction has been started on the new building of the St. Louis County Hospital under a grant from the Federal Government to expand hospital facilities in St. Louis.

During the summer Dr. Robert A. Moore served as Secretary of a Conference Group on Pathology of the National Research Council. This group prepared a Directive for the Army and Navy and was composed of Dr. Ernest W. Goodpasture, Chairman, (Vanderbilt), Dr. Howard T. Karsner (Western Reserve), Dr. Arnold Rich (Johns Hopkins) and Dr. Milton Winternitz (Yale).

First Year Class—July 1943¹

ALABAMA		
Conerly, Ethel Claire	Home Address Jackson	University or College Attended Howard College, Birmingham
ARIZONA		
Austin, Leo Rex	Chandler	University of Arizona, Tucson
Brown, James A.	Tucson	University of Arizona
ARKANSAS		
Geren, Betty B.	Fort Smith	Uni. of Arkansas, Fayetteville
Lambiotte, Louis O.	Fort Smith	University of Arkansas
Ramsey, Robert H.	Fort Smith	University of Arkansas
CALIFORNIA		
Gibson, Jay O.	Litchfield	Uni. of Nevada, Reno, Nevada
Mitchell, Harold H.	Los Angeles	Washington Uni., St. Louis, Mo.
Winkler, R. Kenneth	Fresno	Fresno State College, Fresno
COLORADO		
Everett, Ernest F., Jr.	Fowler	Colorado College, Colo. Springs
IDAHO		
Bond, Robert M.	Lewiston	Washington State College, Pullman, Wash.
Luce, Ralph Raymond	Moscow	University of Idaho, Moscow
Mackey, Oliver M., Jr.	Lewiston	University of Idaho
Marr, James C., Jr.	Boise	Pomona College, Claremont, Cal.
Taylor, Eugene	Moscow	University of Idaho
Thatcher, A. Hal	Preston	University of Idaho
ILLINOIS		
Evans, Edwin R., Jr.	Harrisburg	Washington Uni., St. Louis, Mo.
Ritzmann, Leonard W.	Quincy	Valparaiso Uni., Valparaiso, Ind.
Spitze, Edward C., Jr.	East St. Louis	University of Illinois, Urbana
Sweazy, Donald L.	Cowden	Washington University
Sylvester, Robert F., Jr.	Decatur	James Millikin Uni., Decatur
Tuthill, Sanford W.	Centralia	Washington University
Van Petten, George T.	Marion	Dartmouth Coll., Hanover, N. H.
Watkins, Gladys	Alton	Washington University
Webb, Gerald E.	Harrisburg	Southern Illinois State Normal University, Carbondale
Yost, Paul W.	Lebanon	McKendree College, Lebanon
INDIANA		
Bopp, Henry W., Jr.	Terre Haute	Duke University, Durham, N. C.
KANSAS		
Price, Edwin F., Jr.	Lawrence	University of Kansas, Lawrence
MICHIGAN		
Bentley, Maxwell D.	Royal Oak	Uni. of Idaho, Moscow, Idaho
MINNESOTA		
Smith, Benjamin F., Jr.	Rochester	Carleton College, Northfield
MISSISSIPPI		
Dabbs, Clyde H., Jr.	Tupelo	Millsaps College, Jackson

¹ This list of the class admitted on July 13, 1942 is published in order that the alumni may become acquainted with the students in their localities.

MISSOURI

	<i>Home Address</i>	<i>Univeristy or College Attended</i>
Atwood, John M.	Carrollton	Washington and Lee University, Lexington, Va.
Bates, George Comer	Jefferson City	University of Missouri, Columbia
Beckmann, George E., Jr.	Webster Groves	Washington University, St. Louis
Bergmann, Martin	St. Louis	Washington University
Brereton, Robert L.	Kirkwood	Washington University
Bronson, Shael S.	St. Louis	Washington University
Bussman, Donald W.	St. Louis	Princeton Uni., Princeton, N. J.
Conrad, Marshall B.	Webster Groves	Westminster College, Fulton
Cowdry, Edmund V., Jr.	St. Louis	Princeton Uni., Princeton, N. J.
Edison, Thomas G.	St. Louis	Washington University
Ettleman, Walter I., Jr.	St. Louis	Uni. of New Mexico, Albuquerque
Farrar, John T.	Ladue, St. Louis County	Princeton Uni., Princeton, N. J.
Gantt, Ernest S., Jr.	Jefferson City	Washington University
Gaunt, Frank P.	Webster Groves	Washington University
Giessow, Fred J.	St. Louis	Washington University
Good, James T.	Kansas City	University of Kansas, Lawrence
Herweg, John C.	Springfield	Drury College, Springfield
Jacobs, Charles C., Jr.	St. Louis	Washington University
Johnson, William F.	Ozark	Drury College, Springfield
Johnstone, John T., Jr.	Webster Groves	Westminster College, Fulton
Kalmanson, George M.	St. Louis	Washington University
Kelly, Frank J.	Kansas City	Notre Dame Uni., So. Bend, Ind.
Kilker, Donald E.	Pasadena Hills	Washington University
Koppenbrink, Walter E.	Higginsville	Uni. of Missouri, Columbia
Mehler, Alan H.	St. Louis	Washington University
Polack, Robert T.	Clayton	Washington University
Rapp, Harold B.	North Kansas City	Washington University
Reeves, Gerald A.	Kirksville	Northeast Missouri State Teachers College, Kirksville
Rupe, Clarence E.	Kansas City	Baker Uni., Baldwin, Kan.
Schulz, Clarence G.	St. Charles	Washington University
Tillman, Robert W.	Trenton	William Jewell College, Liberty
Weinhaus, Robert S.	St. Louis	Washington University
Wissner, Seth E.	Normandy	Washington University
Wood, Gary B.	Webster Groves	Washington University

MONTANA

Baltrusch, Oscar W.	Billings	Washington Uni., St. Louis, Mo.
---------------------	----------	---------------------------------

NEVADA

Hood, Thomas Knight	Elko	Pomona College, Claremont, Cal.
---------------------	------	---------------------------------

NEW MEXICO

Prothro, George W.	Clovis	Uni. of New Mexico, Albuquerque
--------------------	--------	---------------------------------

NEW YORK

Guze, Samuel B.	New York	Washington Uni., St. Louis, Mo.
Leight, Leonard	New York	Washington University

OKLAHOMA

Lewis, Ceylon S., Jr.	Muskogee	Washington Uni., St. Louis, Mo.
-----------------------	----------	---------------------------------

PENNSYLVANIA

Ivins, Samuel P.	Chester	Washington Uni., St. Louis, Mo.
------------------	---------	---------------------------------

TENNESSEE

Lockett, Edgar N., Jr.	Johnson City	State Teachers College, Johnson City, Tenn.
------------------------	--------------	---

TEXAS

Smith, Charles G.	Texarkana	Washington Uni., St. Louis, Mo.
-------------------	-----------	---------------------------------

UTAH		
Brown, Roger W.	Home Address Ogden	University or College Attended Uni. of Utah, Salt Lake City
Hall, Robert H.	Salt Lake City	University of Utah
VIRGINIA		
Lanier, Andrew S.	Saluda	Washington and Lee University, Lexington
WASHINGTON		
Berg, Ralph, Jr.	Spokane	State College of Washington, Pullman
Jantz, Walter L.	Walla Walla	Whitman College, Walla Walla
Jayne, Valmor E.	Mansfield	Uni. of Washington, Seattle
Musser, Richard E.	Tacoma	College of Puget Sound, Tacoma
Olson, Arthur J.	Malo	State College of Washington
Ruby, Robert H.	Mabton	Whitworth College, Spokane
WISCONSIN		
Waters, Hugh R.	Wisconsin Rapids	Northwestern Uni., Evanston, Ill.
WYOMING		
Rhodes, Jack R.	Sheridan	Uni. of Wyoming, Laramie

Transfers to the Second Year Class— June, 1942

MISSOURI		
Doyle, Joseph P.	Home Address East Prairie	Medical School Attended University of Missouri, Columbia
Roberts, John P.	Webster Groves	University of Missouri
UTAH		
Nielson, Paul E.	Salt Lake City	University of Wisconsin, Madison

Transfers to the Third Year Class— June, 1942

ALABAMA		
Alford, Almond W.	Home Address Winfield	Medical School Attended University of Alabama
Hodges, William W.	Tuscaloosa	University of Alabama
Pratt, Alsey C., Jr.	Centerville	University of Alabama
Ray, Weldon A.	Tuscaloosa	University of Alabama
Sledge, James N.	Greensboro	University of Alabama
CONNECTICUT		
Spillane, Richard J.	Bloomfield	Dartmouth Medical School
MISSISSIPPI		
Cook, Frederick M.	Clarksdale	University of Mississippi
Jones, William H.	French Camp	University of Mississippi
MISSOURI		
Alex, Morris	St. Joseph	University of Missouri
Alsop, Webb S.	New Franklin	University of Missouri
Dwyer, Frank X.	Kansas City	University of Missouri
Graham, David T.	Clayton	Yale University
Guhleman, Henry	Jefferson City	University of Missouri
Haddock, James N.	Cape Girardeau	University of Missouri
Kennedy, Walter J.	Sedalia	University of Missouri

	<i>Home Address</i>	<i>Medical School Attended</i>
Meyn, M. Faye	Mt. Vernon	University of Missouri
Motley, Cornealia E.	Columbia	University of Missouri
Parker, H. Graham	Kansas City	University of Missouri
Sudholt, Alfred F., Jr.	St. Louis	University of Missouri
Welborn, William S.	St. Louis	University of Missouri
Westcott, Robert J.	Knox City	University of Missouri
<i>NORTH CAROLINA</i>		
Allen J. Harry	Reidsville	University of North Carolina
Costner, Alfred N.	Lincolnton	University of North Carolina
Rose, Ira	Rocky Mount	University of North Carolina
<i>NORTH DAKOTA</i>		
Finsten, Herman L.	Grand Forks	University of North Dakota
<i>SOUTH DAKOTA</i>		
Geppert, Joseph W.	Vermillion	University of South Dakota
Geppert, Thomas V.	Vermillion	University of South Dakota
Ramsdell, Stuart	Flandreau	University of South Dakota
<i>UTAH</i>		
Larsen, Boyd	Lehi	University of Utah
Woolsey, Carl T.	Salt Lake City	University of Utah
<i>WEST VIRGINIA</i>		
Quick, James C.	Clendenin	West Virginia University
Vest, James C.	Whitesville	West Virginia University
<i>ENGLAND</i>		
Oleesky, Samuel	Manchester	Manchester University

News of Alumni

Seymour Brown, Lt. (MC), USN, was a member of the graduating class of 1940. For the past several months he has been the medical officer aboard the U. S. S. Benham. He writes that his work has been very interesting both from a medical and military viewpoint. To prove this statement the following excerpt is taken from a recent letter:

"A little over a month ago, I had to perform an appendectomy aboard—on the wardroom table. It is a rare occurrence as one tries to transfer such patients to larger ships, but this was impossible at the time. I had no retractors and made some from bent table forks and a couple pieces of aluminum we found. These were too pliable and kept bending. It was a 'red hot' retrocecal appendix! My first assistant was a hospital corpsman who had never been an assistant on a major operation before, so I had to do all the work. In addition he fainted when we were only a third finished. I used my 1st class pharmacist mate as anesthetist to administer intravenous sodium pentothal. I was afraid to use ether because it was very hot with too many fires nearby; spinal anesthesia was impossible because of the rolling of the ship. We didn't get good relaxation despite the article in the A. M. A. We had no fluids suitable for i. v. use, so the engineer rigged up a little distilling apparatus which ran all night to distill water. Luckily there were a couple bottles of powdered human plasma aboard which were very useful, both for the plasma and the accompanying i. v. set. Also had some sulfathiazol tablets. Incidentally, the officers were peeking in the pantry window so that a running account was passed on through the ship during operation. The patient was eating solid food on the fourth day and walking on the seventh."

1899

J. B. Woodson is Superintendent and Medical Director of the Piedmont Sanatorium in Burkeville, Va.

1904

J. J. Singer has been appointed Medical Director for the Los Angeles Sanatorium at Duarte, Calif. Dr. Singer is also president of the tuberculosis section of the Los Angeles County Medical Society, director of the Rose Lampert Graff Foundation, a tuberculosis research organization, and associate clinical professor of medicine at the University of Southern California.

1905

Robert A. Schlernitzauer is in the "orange growing and private order citrus fruit shipping business." Dr. Schlernitzauer retired after practicing medicine for 25 years in Rockledge,

Florida. However, he is now serving with the Auxilliary Coast Guard. He writes that he would like very much to see some old friends if they are ever in his vicinity.

1919

Lloyd J. Thompson, Yale University School of Medicine, New Haven, Conn. holds the rank of Lieutenant Colonel in the Army Medical Corps. Col. Thompson was a member of the Student Army Training Corps in 1918.

1920

Lt. Col. H. L. White's address is Station Hospital, A. P. O. 945, c/o Postmaster, Seattle, Wash. Col. White is former editor of the Alumni Quarterly.

1922

William J. Dieckmann has been appointed professor of obstetrics and gynecology in the School of Medicine

of the University of Chicago, and gynecologist-in-chief of two hospitals affiliated with the university. Dr. Dieckmann was associate professor of obstetrics and gynecology and also was a former faculty member of the Washington University School of Medicine.

1924

Major Milo K. Tedstrom is now serving with the U. S. Air Corps and stationed at Mather Field, Calif.

1925

Lt. Comdr. Hugo O. Wagner gives as his address U. S. S. Wright, c/o Fleet Post Office, San Francisco, Calif.

Jerome S. Levy, Little Rock, Ark., has been called to active duty as Captain, Army Medical Corps, and assigned to William Beaumont General Hospital, Fort Bliss, Texas.

1926

Henry Rover was recently commissioned Lieut. Comdr., U. S. N., and is stationed at San Diego.

John Milton McCaughan is a member of the faculty of the St. Louis University School of Medicine in the Department of Surgery.

1927

Captain Colby Hall is stationed at Sawtelle, Calif., with the 67th Evacuation Hospital.

L. N. Claiborn holds the rank of Major in the Army Medical Corps and is attached to the 39th General Hospital (Yale Unit) in charge of plastic surgery.

1928

Col. Wilford F. Hall holds the rating of Flight Surgeon in the Army Air Force. Col. Hall has been with the Air Forces since January, 1935, and his present duty assignment is that of Chief of Personnel Division, Air Surgeon's Office, Washington, D. C.

Major A. Lloyd Stockwell is stationed at the O'Reilly General Hospital, Springfield, Mo.

C. L. Hudiburg has offices in the

Medical Arts Bldg., Wilmington, Delaware, and specializes in obstetrics and gynecology. He writes that a few weeks ago he delivered 8 babies in 22 hours.

A bulletin from the Office of Director Naval Officer Procurement in Los Angeles is signed by G. E. Helmkamp, Lieut. Comdr. (M. C.), U. S. N. R.

1929

Lt. Col. James H. Forsee is Commanding Officer of the 2nd Auxiliary Surgical Group, Lawson General Hospital, Atlanta, Ga.

Dr. and Mr. Arthur W. Hankwitz are announcing the birth of a son, John Elliott, in Milwaukee on August 27, 1942. John Elliott has two older brothers, Frederick Paul and Carl Arthur.

1932

Lieut. Comdr. Wendell G. Scott is stationed at the U. S. Naval Air Station, Family Hospital, San Diego, Calif.

1933

James W. Bagby, Lt. (M. C.) is at the Great Lakes Naval Training Station, Great Lakes, Ill. Lt. Bagby is Secretary-Treasurer of the Alumni Association, but his duties have been assumed for the duration by the Acting Secretary - Treasurer, Dr. Rogers Deakin, '22.

1934

Everett S. Sanderson, Medical College, University of Georgia, Augusta, is a member of the Social Protective Committee and was recently elected president of the Augusta Tuberculosis Association. Dr. Sanderson writes that classmates and alumni who are in the armed forces—or out of them—who may be in that area are welcome at the above address or at his home, 1630 Katherine St., Augusta, Ga.

Samuel Schwartz is engaged in the practice of pediatrics at 1028 Connecticut Ave., N. W., Washington, D. C. Dr. Schwartz is a Fellow of the American Academy of Pediatricians and has re-

cently joined the faculty of Georgetown University as a Clinical Instructor in Pediatrics.

1935

Major Bert Bradford, Jr., is with the 45th Evacuation Hospital, Camp Gordon, Ga.

Charles Lee Hoagland is an associate member of the Rockefeller Institute in New York City.

1936

The promotion of John W. Records from Captain to Major in the Army Medical Corps was announced August 24 at headquarters of the Medical Field Service School, Carlisle Barracks, Pa., where Major Records is on duty in the Department of Logistics.

Major and Mrs. O. E. Ursin announce the birth of a son, Nikolai Elliott, on June 15. Major Ursin is a member of the staff of the Medical Field Service School, Carlisle Barracks, Pa. This summer he attended the Command and General Staff School at Fort Leavenworth, Kans.

1937

Joseph A. Fiorito has announced the opening of an office for the practice of obstetrics and gynecology at 303 Whitney Ave., New Haven, Conn.

Capt. Bernard Alan Cruvant, Station

Hospital, Fort Belvoir, Va., is Assistant Medical Officer there. He writes that he is getting some fascinating and valuable training, especially in psychoneuroses, and would like to trade experiences with others doing psychiatric work in the Army.

Marie H. Wittler is entering private practice in pediatrics at Elmhurst and Glen Ellyn, Illinois, suburbs of Chicago. Dr. Wittler's address is 105 S. York St., Elmhurst, Ill.

1938

Captain Eugene R. Melaville is with the 306th Medical Battalion, 81st Division stationed at Camp Rucker, Alabama.

1940

John E. Gallagher and Margaret E. Jondro of Detroit, Mich., were married July 2. Dr. Gallagher is doing general practice in the office left by his father, the late Joseph Charles Gallagher, '01, at Rossford, Ohio.

Mary B. Johnson is an associate in practice with Dr. Herman P. Gunner of Berwyn, Ill.

1941

Ruth C. Martin is in the Department of Anesthesia, University Clinics, University of Chicago.

***Buy War Stamps and Bonds
Then Contribute to Alumni Fund***

Student News

The following statement was read at the exercises on the opening of school on the evening of July 13. "A university is indeed fortunate if the fraternities and student organizations take an active part in the promotion of scholarship. In the Washington University School of Medicine the Phi Beta Pi Fraternity has for some years sponsored an annual lectureship in honor of the emeritus professor of pathology, Dr. Leo Loeb. The local chapter of Alpha Omega Alpha brings to St. Louis each year a distinguished lecturer, and awards a prize for student research. This spring the Alpha Kappa Phi Chapter of Nu Sigma Nu established two permanent annual awards. A Committee of the Faculty was instructed to select the outstanding freshman and the outstanding sophomore, on the basis of scholarship, character, leadership, personality, and extracurricular activities."

"It is my privilege, this evening, Mr. Dean, to present Mr. David Talmadge and Mr. Edwin Krebs as the recipients of the first Nu Sigma Nu Awards as the outstanding students in the first and second year classes. During their residency in the Washington University School of Medicine, both have held a Jackson Johnson scholarship."

"Mr. Talmadge was born in Korea, the son of a Presbyterian missionary. After attendance at the Pyengyang Foreign School in Korea, he was graduated from Davidson College in June, 1941, with the degree of Bachelor of Arts, summa cum laude. He was valedictorian and stood second in a class of 135. As a student in this Medical School he stood first in a class of 74 and was awarded honors in Anatomy, Histology, and Biochemistry. The Committee nominates Mr. Talmadge for the

Nu Sigma Nu Award, as the outstanding student in the first year class."

"Mr. Krebs comes from Greenville, Illinois, and is also the son of a Presbyterian minister. Parenthetically, it appears that the Presbyterian faith engenders good scholarship as well as good Christianity. Mr. Krebs graduated from the Urbana High School and in June 1940 from the University of Illinois—the third son of a widowed mother to graduate from the University with high honors—truly eloquent testimony to the faith and ambition of these boys and their mother. The record shows that of 133 hours of credit during the 4 years of college he attained the grade of A in 120. In the Department of Chemistry, in which he majored, he secured 4.9 credits per semester hour out of a possible 5. As a first year medical student he served as a student assistant in biochemistry, and stood twelfth in a class of 80. In the second year of medicine he stood first in a class of 83, and has been awarded honors in Biochemistry, Bacteriology, Physiology, Pathology, and Pharmacology. The Committee nominates Mr. Krebs for the Nu Sigma Nu Award as the outstanding student of the second year class."

Under the will of the late Mr. Jackson Johnson of the International Shoe Company, the sum of \$250,000 was given to the University, the income to be used "to aid worthy and desirable students in acquiring and completing their medical education." The income of this fund is now being devoted mainly to Honor Scholarships named for the donor.

The purpose of the Jackson Johnson Scholarships is to enable students of exceptional ability and performance, re-

ardless of their financial resources, to enter upon training for careers in medicine and medical sciences. The awards are restricted to those judged to possess definitely superior talents and qualifications, and are made initially only to applicants accepted for the first year class in the School of Medicine. The award may be continued for each of the later years of the course, provided the quality of the student's work justifies it.

These scholarships were awarded for the first time in 1937. During the period from 1937 to 1942, thirty-four students have received these scholarships. At the present time, twenty-two members of the student body hold Jackson Johnson Awards, including four members of the new freshman class.

1. *Ernest Frank Everett, Jr.*, of Fowler, Colorado. He attended Colorado College, receiving the degree of Bachelor of Arts, in 1942. He is a member of Phi Beta Kappa. For three years he was student assistant in Biology at Colorado College.

2. *Edwin Fletcher Price, Jr.*, of Lawrence, Kansas. He attended the

University of Kansas, receiving the degree of Bachelor of Arts in 1942, and is a member of Phi Beta Kappa.

3. *Leonard Walter Ritzmann*, of Quincy, Illinois. He attended Valparaiso University at Valparaiso, Indiana, receiving the degree of Bachelor of Arts in 1942. He was student assistant in Biology for three years.

4. *Clarence Rupe*, of Topeka, Kansas. He attended Baker University at Baldwin, Kansas, receiving his Bachelor of Arts degree in 1941. He was a student assistant in Biology at Baker University.

Although the summer in St. Louis was not as hot as usual (!), the air-conditioned rooms for lectures were most welcome. The room off the balcony of the Autopsy Amphitheatre was renovated and arranged as a study room for students and staff. A current museum of photomicrographs, gross specimens and radiographs is maintained in this room. A techniscope was purchased and is available for instruction of small groups.

Shortage of Microscopes

It is highly probable that during the next few years students will not be able to purchase new microscopes. Alumni, who have no need for their microscopes, can help in a solution of this problem. Mr. James J. Ritterskamp, Purchasing Agent of the University, will be pleased to hear from alumni and arrange to purchase used modern microscopes.

WASHINGTON UNIVERSITY

George R. Throop, Ph.D., LL.D., Bridge Chancellor

Walter E. McCourt, A.M., Assistant Chancellor

The College of Liberal Arts
William G. Bowling, A.M., Dean

The School of Engineering
Alexander S. Langsdorf, M.M.E., Dean

The School of Architecture
Alexander S. Langsdorf, M.M.E., Dean

The School of Business and Public Administration
William H. Stead, Ph.D., Dean

The Henry Shaw School of Botany
George T. Moore, Ph.D., Director

The School of Graduate Studies
Richard F. Jones, Ph.D., Dean

The School of Law
Warner Fuller, B.S., LL.B., Acting Dean

The School of Medicine
Philip A. Shaffer, Ph.D., Dean

The School of Dentistry
Benno E. Lischer, D.M.D., Dean

The School of Nursing
Louise Knapp, B.S., A.M., Director

The School of Fine Arts
Kenneth E. Hudson, B.F.A., Director

The University College
Willis H. Reals, Ph.D., Acting Dean

The Summer School
Frank L. Wright, A.M., Ed.D., Director

Mary Institute, a preparatory school for girls, located at Ladue and Warson Roads, is also conducted under the charter of the University.

Note: Complete information about any of the schools listed above may be obtained by writing to the Dean or Director concerned.